1

Qué consideramos efectivo en los estudios de IT oral.

Evaluation of clinical outcomes of efficacy in food allergen immunotherapy trials, COFAITH EAACI task force.

Rodríguez Del Río P, Álvaro-Lozano M, Arasi S, Bazire R, Escudero C, Patel N et al

Allergy. 2024 Jan 23. doi: 10.1111/all.16027. Epub ahead of print. PMID: 38263695.

ABSTRACT

Food allergy is a global public health problem that until recent years lacked any aetiological treatment supported by academy, industry and regulators. Food immunotherapy (AIT) is an evolving treatment option, supported by clinical practice and industry trial data. Recent AIT metaanalyses have highlighted the difficulty in pooling safety and efficacy data from AIT trials, due to secondary heterogeneity in the study. An EAACI task force (CO-FAITH) initiated by the Paediatric Section was created to focus on AIT efficacy outcomes for milk, egg and peanut allergy rather than in trial results. A systematic search and a narrative review of AIT controlled clinical trials and large case series was conducted. A total of 63 manuscripts met inclusion criteria, corresponding to 23, 21 and 22 studies of milk, egg and peanut AIT, respectively. The most common AIT efficacy outcome was desensitization, mostly defined as tolerating a maintenance phase dose, or reaching a particular dose upon successful exit oral food challenge (OFC). However, a large degree of heterogeneity was identified regarding the dose quantity defining this outcome. Sustained unresponsiveness and patientreported outcomes (e.g. quality of life) were explored less frequently, and to date have been most rigorously described for peanut AIT versus other allergens. Change in allergen threshold assessed by OFC remains the most common efficacy measure, but OFC methods suffer from heterogeneity and methodological disparity. This review has identified multiple heterogeneous outcomes related to measuring the efficacy of AIT. Efforts to better standardize and harmonize which outcomes, and how to measure them must be carried out to help in the clinical development of safe and efficacious food allergy treatments.

2

Tiremos de registro y comprobemos la efectividad de la ITA de los últimos 20 años en Dinamarca.

The effectiveness of pollen allergen immunotherapy on allergic rhinitis over 18 years: A national cohort study in Denmark.

Bager P, Poulsen G, Wohlfahrt J, Melbye M

Allergy. 2024 Jan 21. doi: 10.1111/all.16026. Epub ahead of print. PMID: 38247235.

BACKGROUND

Because long-term effectiveness of pollen allergen immune therapy (AIT) for allergic rhinitis (AR) is not well-described, we studied effectiveness over 18 years in Denmark.

METHODS

A register-based cohort study using data on filled prescriptions, 1995-2016, Denmark. In a cohort of 1.1 million intranasal corticosteroid inhaler users (proxy for AR), we matched users treated with grass, birch or mugwort AIT 1:2 with non-treated users on baseline year and 24 characteristics in the 3 years prior to baseline. The primary outcome was the odds ratio (OR) of using anti-allergic nasal inhaler during the pollen season in the treated versus non-treated group by years since baseline.

RESULTS

Among 7760 AR patients treated with pollen AIT, the OR of using nasal inhaler 0-5 years after baseline was reduced when compared with 15,520 non-treated AR individuals (0-2 years, OR 0.84 (0.81-0.88); 3-5 years, OR 0.88 (0.84-0.92)), but was close to unity or higher thereafter (6-9 years, OR 1.03 (0.97-1.08); 10-18 years, OR 1.18 (1.11 1.26)). In post hoc analyses, results were more consistent for those who already had 3 of 3 baseline years of use, and in patients using nasal inhaler in the latest pollen season (0-2 years, OR 0.76 (0.72-0.79); 3-5 years OR 0.86 (0.81-0.93); 6-9 years, OR 0.94 (0.87-1.02); 10-18 years, OR 0.94 (0.86 1.04)) as opposed to no such use.

CONCLUSIONS

Patients treated with pollen AIT in routine care to a higher degree stopped using anti-allergic nasal inhaler 0-5 years after starting the standard 3 years of therapy, and not beyond 5 years. Post hoc analyses suggested effectiveness was more consistent among patients with persistent AR.

3

Cambios inmunológicos en ITA con alergoide confirmados por transcriptómica.

Peripheral blood mononuclear cell transcriptome profile in a clinical trial with subcutaneous, grass pollen allergoid immunotherapy.

Starchenka S, Oluwayi K, Heath M, Armfield O, Shamji M et al

Clin Exp Allergy. 2024 Jan 2. doi: 10.1111/cea.14432. Epub ahead of print. PMID: 38169056.

INTRODUCTION

Allergen-specific immunotherapy (AIT) is the only disease-modifying treatment in allergic airway diseases. Underlying immunological mechanisms and candidate biomarkers, which may be translated into predictive/surrogate measures of clinical efficacy, remain an active area of research. The aim of this study was to evaluate Pollinex Quattro (PQ) Grass AIT induced immunomodulatory mechanisms, based on transcriptome profiling of peripheral blood mononuclear cells.

METHODS

119 subjects with grass pollen induced seasonal allergic rhinitis (SAR) were randomized in a 2:2:1:1 ratio to receive a cumulative dose of PQ Grass as a conventional or extended pre-seasonal regimen, placebo, or placebo with MicroCrystalline Tyrosine. Gene expression analysis was an exploratory endpoint evaluated in a subgroup of 30 subjects randomly selected from the four treatment arms. Samples were collected at three time points: screening (baseline), before the start of the grass pollen season and at the end of the season. This study was funded by the manufacturer of PQ.

RESULTS

Transcriptome analysis demonstrated that the most significant changes in gene expression, for both treatment regimens, were at the end of the grass pollen season, with the main Th1 candidate molecules (IL-12A, IFNγ) upregulated and Th2 signature cytokines downregulated (IL-4, IL-13, IL-9) ($p < .05$). Canonical pathways analysis demonstrated Th1, Th2, Th17 and IL-17 as the most significantly enriched pathways based on absolute value of activation z-score (|z| score ≥ 2, $p < .05$). Upstream regulator analysis showed pronounced inhibition of pro-inflammatory allergic molecules IgE, IL-17A, IL-17F, IL-25 (IL-17E) (|z| score ≥ 2, FDR < 0.05) and activation of pro-tolerogenic molecules IL-12A, IL-27, IL-35 (EBI3) at the end of the grass pollen season.

CONCLUSION

Peripheral blood mononuclear cells transcriptome profile showed an inhibition of Th2, Th17 pro inflammatory allergic responses and immune deviation towards Th1 responses. PQ Grass extended regimen exhibited a superior mechanistic efficacy profile in comparison with PQ conventional regimen.

4

Expresión génica tras ITA: mejor tras ITA + dupilumab que tras ITA sola.

Differential modulation of allergic rhinitis nasal transcriptome by dupilumab and allergy immunotherapy.

Wipperman MF, Gayvert KM, Atanasio A, Wang CQ, Corren J et al

Allergy. 2024 Jan 27. doi: 10.1111/all.16001. Epub ahead of print. PMID: 38279910.

BACKGROUND

Nasal epithelial cells are important regulators of barrier function and immune signaling; however, in allergic rhinitis (AR) these functions can be disrupted by inflammatory mediators. We aimed to better discern AR disease mechanisms using transcriptome data from nasal brushing samples from individuals with and without AR.

METHODS

Data were drawn from a feasibility study of individuals with and without AR to Timothy grass and from a clinical trial evaluating 16 weeks of treatment with the following: dupilumab, a monoclonal antibody that binds interleukin (IL)-4Rα and inhibits type 2 inflammation by blocking signaling of both IL-4/IL-13; subcutaneous immunotherapy with Timothy grass (SCIT), which inhibits allergic responses through pleiotropic effects; SCIT + dupilumab; or placebo. Using nasal brushing samples from these studies, we defined distinct gene signatures in nasal tissue of AR disease and after nasal allergen challenge (NAC) and assessed how these signatures were modulated by study drug(s).

RESULTS

Treatment with dupilumab (normalized enrichment score [NES] = -1.73, $p = .002$) or SCIT + dupilumab (NES = -2.55, $p < .001$), but not SCIT alone (NES = +1.16, $p = .107$), significantly repressed the AR disease signature. Dupilumab (NES = -2.55, $p < .001$), SCIT (NES = -2.99, $p < .001$), and SCIT + dupilumab (NES = -3.15, $p < .001$) all repressed the NAC gene signature.

CONCLUSION

These results demonstrate type 2 inflammation is an important contributor to the pathophysiology of AR disease and that inhibition of the type 2 pathway with dupilumab may normalize nasal tissue gene expression.

5

Efectividad y calidad percibida de los comprimidos de ácaros (300 IR).

Clinical benefits with 300 IR HDM SLIT tablet in Europeans with house dust mite allergic rhinitis: Post hoc analysis of a large phase 3 trial.

Pfaar O, De Blay F, Canonica GW, Casale TB, Gevaert P, et al

World Allergy Organ J. 2023 Dec 22;17(1):100849. PMID: 38225952.

BACKGROUND

House dust mite (HDM)-induced allergic rhinitis (AR) is a major cause of allergic respiratory disease. The efficacy and safety of the 300 IR HDM sublingual immunotherapy (SLIT) tablet in patients with moderate-to-severe HDM-AR was confirmed in a large, international, phase 3 randomized controlled trials (RCTs). Here, we analyzed the results in the European population.

METHODS

Data from 91 European centers that participated in the international, double-blind, RCT (EudraCT 2014-004223- 46, NCT02443805) with the 300 IR HDM SLIT tablet versus placebo over 12 months were analyzed post hoc. The treatment effect in European adults and adolescents was notably assessed through the European Academy of Allergy and Clinical Immunology (EAACI)- recommended combined symptom and medication score (CSMS0-6 , pre-defined endpoint) and the total combined rhinitis score (TCRS0-24, post hoc endpoint, also balanced) during the primary evaluation period (4 weeks at the end of treatment period) using analysis of covariance (ANCOVA).

RESULTS

There were 818 patients who comprised the modified full analysis set in Europe. Over the primary period, the differences in CSMS0-6 and TCRS0-24 between the 300 IR and placebo groups were statistically significant ($p < 0.0001$): -0.32 (95%CI [-0.46; -0.17]) and - 1.28 (95%CI [-1.63; -0.94]), respectively, with relative differences of -20.9% and -21.2%. All post hoc and the rhinoconjunctivitis quality of life endpoints were significantly improved with 300 IR versus placebo. The 300 IR HDM tablet was generally well tolerated.

CONCLUSION

This RCT sub-analysis confirmed the 300 IR HDM SLIT tablet is an effective and safe treatment for European adults and adolescents with HDM-AR with clinically meaningful benefits from the patients' perspective. Trial registration: NCT02443805. Registered on April 29, 2015./EudraCT 2014-004223-46. Registered on September 16, 2015.

6

Da igual a qué sea tu alergia, la ITA con comprimidos (SQ) funciona y mejora tu calidad de vida.

Sublingual tablet immunotherapy improves quality of life in adults with allergic rhinoconjunctivitis.

Blaiss MS, Durham SR, Bernstein D, Stranzl T, Lindholm M, et al

J Allergy Clin Immunol Pract. 2024 Jan 31:S2213-2198(24)00140-5. Epub ahead of print. PMID: 38307205.

BACKGROUND

Allergic rhinitis with or without conjunctivitis (AR/C) can negatively impact many aspects of quality of life (QoL). The efficacy and safety of SQ sublingual immunotherapy (SLIT)-tablets have been confirmed across large clinical trials in adults with grass, tree, ragweed, and house dust mite (HDM) AR/C.

OBJECTIVE

This pooled analysis investigates whether the reduction in symptom burden found across the clinical trials is supported by improvements in QoL.

METHODS

11 phase II/III randomized placebo-controlled trials across the SQ grass, tree, ragweed and HDM SLIT tablets (Grass: N=3179; Ragweed: N=767; Tree: N=634; HDM: N=2221) were included. QoL was assessed using the standardized Rhinitis Quality of Life Questionnaire (RQLQ) with the exception of three grass trials that used the non-standardized version. The overall RQLQ scores were expressed as a mean of seven domains. In the pooled analysis, treatment was used as fixed effect; the trial, and the interaction between region/country with the trial as random effects.

RESULTS

The pooled analysis showed consistent and statistically significant improvements in overall RQLQ scores across all four SQ SLITtablets vs. placebo (Pooled estimate [95%CI], p value. Grass: -0.20 [-0.28, -0.12], P<0.001. Tree: -0.42 [-0.58, -0.26], P<0.001. Ragweed: - 0.36 [-0.55, -0.17], P<0.001. HDM: -0.28 [-0.39, -0.17], P<0.001). Furthermore, significant improvements vs. placebo for all four SQ SLITtablets were seen across the 7 individual domains.

CONCLUSION

The proven efficacy of SQ SLIT-tablets to reduce symptoms across four of the most common respiratory allergens, is supported by concurrent significant improvements in RQLQ scores - overall and for all 7 domains.

7

La SLIT mejora tu día a día aquí ... y en Japón.

Effectiveness of sublingual immunotherapy in pediatric cedar pollinosis: A real-world database study.

Matsushita R, Tanaka-Mizuno S, Takeuchi M, Kawakami K

Pediatr Allergy Immunol. 2024 Jan;35(1):e14075. doi: 10.1111/pai.14075. PMID: 38284920.

BACKGROUND

Pediatric allergic rhinitis (AR), including cedar pollinosis (CP), is increasing in Japan. We investigated the effects of sublingual immunotherapy (SLIT), which has limited studies of its effectiveness in real-world settings, on children with CP.

METHODS

This retrospective cohort study used a claim database in 2018-2021. Children aged ≤15 years with CP records in 2019 were eligible and were followed up through 2021. We included 2962 CP children undergoing SLIT and 547 who were not. The medication score was used to evaluate SLIT effectiveness in the cedar pollen dispersal season each year. Adverse events and the occurrence of allergic diseases were also evaluated.

RESULTS

Medication score was higher in the SLIT group during the index period but lower in 2021 compared to the non-SLIT group (mean ± standard deviation: 5.17 ± 2.39 and 4.74 ± 2.38 in 2019, 3.13 ± 2.30 and 3.55 ± 2.48 in 2021, respectively). The adjusted mean difference between groups from 2019 to 2021 was -0.62 (95% confidence interval: -0.86 to -0.39, p < .0001), and the medication score was reduced in the SLIT group (risk ratio: 1.2: 1.1 to 1.3). The occurrence of adverse events involving abdominal disorders (adjusted odds ratio [aOR]: 0.64: 0.51 to 0.81), asthma exacerbation (aOR: 0.37: 0.24 to 0.57), and allergic diseases involving hay fever unrelated to CP (aOR: 0.60: 0.45 to 0.80) or asthma (aOR: 0.71: 0.58 to 0.86) was lower in the SLIT group.

CONCLUSION

In children with CP, SLIT is effective, well tolerated, and could decrease the occurrence of other allergic diseases.

8

Síndrome polen-frutas: dime alérgeno responsable y te diré qué evitar.

Diagnosis and Management of Pollen-Food Allergy Syndrome to Nuts.

Giovannini M, Skypala IJ, Caubet JC, Du Toit G, Nowak-Wegrzyn A

J Allergy Clin Immunol Pract. 2024 Jan 25:S2213-2198(24)00077-1. Epub ahead of print. PMID: 38280450.

ABSTRACT

Oral Allergy Syndrome (OAS), or Pollen Food Allergy Syndrome (PFAS) represents a common clinical conundrum when the reported trigger food is a tree nut (usually almond or hazelnut) or peanut. The PFAS may give rise to uncertainty about the potential severity of the future reactions, indications for prescribing epinephrine, and the extent of the necessary dietary avoidance. As a food allergy, secondary to cross-reactivity with airborne pollen, PFAS usually manifests towards the end of the first decade of life as contact urticaria of the oropharyngeal mucous membranes. Molecular allergology facilitates diagnosis and risk stratification by establishing the profile of sensitization. Exclusive sensitization to PR10 and profilins indicates signs and symptoms are due to PFAS, whereas sensitization to seed storage proteins with or without sensitization to PR10 and profilins may indicate a more severe primary nut allergy phenotype. Management relies on avoidance of the specific nut trigger, advice on the likelihood of more severe local or systemic symptoms, and treatment of reactions according to the severity. Future studies are needed to better delineate the risk of systemic reactions in individuals with nut PFAS, and to establish the role of food or pollen allergen immunotherapy for the prevention or moderation of this condition.

9

Piel: puerta de entrada y objetivo a controlar.

Skin as the Target for Allergy Prevention and Treatment.

Marques-Mejias A, Bartha I, Ciaccio CE, Chinthrajah RS, Chan S, et al

Ann Allergy Asthma Immunol. 2024 Jan 20:S1081-1206(24)00001-2. Epub ahead of print. PMID: 38253125.

ABSTRACT

The fact that genetic and environmental factors could trigger disruption of the epithelial barrier and subsequently initiate a Th2 inflammatory cascade conversely proposes that protecting the same barrier and promoting adequate interactions with other organs, like the gut, may be crucial for lowering the risk and preventing atopic diseases particularly, food allergies. In this review, we provide an overview of structural characteristics that support the epithelial barrier hypothesis in AD patients, including the most relevant filaggrin gene mutations, the recent discovery of the role of the transient receptor potential vanilloid 1 (TRPV1), and the role involvement of the microbiome in healthy and damaged skin. We present experimental and human studies that support the mechanisms of allergen penetration, particularly the dual allergen exposure and the outside-in, inside-out, and outside-inside-outside hypotheses. We discuss classic skin-targeted therapies for food allergy prevention, including moisturizers, steroids, and TCI, along with pioneering trials proposed to change their current use (PACI and SEAL). We provide an overview of the novel therapies that enhance the skin barrier, like probiotics and prebiotics topical application, read-through drugs, direct and indirect FLG replacement, and IL and JAK inhibitors. Lastly, we discuss the newer strategies for preventing and treating food allergies in the form of epicutaneous immunotherapy (EPIT) and the experimental use of single-dose of adeno-associated virus (AAV) vector gene immunotherapy.

10

¿Y si la ITA previene la aparición de enfermedades autoinmunes?

Effect of sublingual immunotherapy on clinical and laboratory autoimmunity.

Bozek A, Mućka S, Miodonska M, Zlik A, Mroz-Dybowska M

Immunotherapy. 2024 Jan 12. doi: 10.2217/imt-2023-0231. Epub ahead of print. PMID: 38214133.

BACKGROUND

There still are few data on the long-term safety of sublingual immunotherapy (SLIT). The aim of this study was to assess the appearance of autoimmune diseases in patients before and after SLIT.

MATERIALS AND METHODS

New cases of autoimmune diseases were monitored. Patients in the SLIT group (n = 816) were compared with controls (n = 1096).

RESULTS

The new incidences of autoimmune diseases in the SLIT group were lower compared with the control group: 18 (2.2%) versus 58 (5.3%); $p < 0.05$. Systemic lupus erythematosus, psoriasis and Hashimoto appeared much more often in the control group.

CONCLUSION

SLIT had no significant effect on the induction of autoimmune diseases.

1

La combinación de biomarcadores predice mejor la respuesta a ITA.

Immune signatures predict response to house dust mite subcutaneous immunotherapy in patients with allergic rhinitis.

Nan Wang, Jia Song, Shi-Ran, Ke-Zhang Z, Jing-Xian Li, Zhi-Chao Wang , Cui-Lian Guo et al.

Allergy . 2024 Feb 25.doi: 10.1111/all.16068.

BACKGROUND

Identifying predictive biomarkers for allergen immunotherapy response is crucial for enhancing clinical efficacy. This study aims to identify such biomarkers in patients with allergic rhinitis (AR) undergoing subcutaneous immunotherapy (SCIT) for house dust mite allergy.

METHODS

The Tongji (discovery) cohort comprised 72 AR patients who completed 1-year SCIT follow-up. Circulating T and B cell subsets were characterized using multiplexed flow cytometry before SCIT. Serum immunoglobulin levels and combined symptom and medication score (CSMS) were assessed before and after 12-month SCIT. Responders, exhibiting ≥30% CSMS improvement, were identified. The random forest algorithm and logistic regression analysis were used to select biomarkers and establish predictive models for SCIT efficacy in the Tongji cohort, which was validated in another Wisco cohort with 43 AR patients.

RESULTS

Positive SCIT response correlated with higher baseline CSMS, allergen-specific IgE (sIgE)/total IgE (tIgE) ratio, and frequencies of Type 2 helper T cells, Type 2 follicular helper T (TFH 2) cells, and CD23+ nonswitched memory B (BNSM) and switched memory B (BSM) cells, as well as lower follicular regulatory T (TFR) cell frequency and TFR /TFH 2 cell ratio. The random forest algorithm identified sIgE/tIgE ratio, TFR /TFH 2 cell ratio, and BNSM frequency as the key biomarkers discriminating responders from nonresponders in the Tongji cohort. Logistic regression analysis confirmed the predictive value of a combination model, including sIgE/tIgE ratio, TFR /TFH 2 cell ratio, and CD23+ BSM frequency (AUC = 0.899 in Tongji; validated AUC = 0.893 in Wisco).

CONCLUSIONS

A T- and B-cell signature combination efficiently identified SCIT responders before treatment, enabling personalized approaches for AR patients.

2

IT con plásmidos de DNA en alergia a cacahuete.

Safety and immunopharmacology of ASP0892 in adults or adolescents with peanut allergy: two randomized trials.

Brian C Ferslew, Ronald Smulders, Tong Zhu, Mary B Blauwet, Tomohiro Kusawake, Anna Spence et al.

Allergy. 2024 Feb;79(2):456-470.doi: 10.1111/all.15931.

BACKGROUND

New treatment options with improved safety and novel mechanisms of actions are needed for patients with peanut allergy.

OBJECTIVES

To evaluate the safety, tolerability, and immunogenicity of ASP0892, a peanut DNA vaccine, after intradermal (id) or intramuscular (im) administration in adult or adolescent patients with peanut allergy in two phase 1 studies.

METHODS

ASP0892 or placebo was administered every 2 weeks for a total of 4 doses. The doses were 1 mg or 4 mg id or 4 mg im for adults, and 1 mg or 4 mg id for adolescents. Immunologic parameters were assessed longitudinally.

RESULTS

Thirty-one adults (mean age 24.3 years, 17 males) received ASP0892 (9, 8, 8 patients for 1 mg id, 4 mg id or 4 mg im, respectively) or placebo (2 patients/group). Twenty adolescents (mean age 14.2 years, 11 males) received ASP0892 (8 patients/group) or placebo (2 patients/group). In both studies, the most common treatment-emergent adverse event (TEAE) was injection site pruritus. No deaths or treatment withdrawal were related to TEAEs. No serious TEAEs related to treatment were observed in adult or adolescent patients. ASP0892 treatment led to modest increases in allergen-specific IgG and/or IgG4 in adults (1 mg id, 4 mg im) and adolescents (1 mg id, 4 mg id). No improvements in clinical outcomes, including double blind placebo-controlled food challenge, were found after ASP0892 treatment.

CONCLUSIONS

In two phase 1 studies, ASP0892 was well tolerated with modest but not clinically relevant changes in immune responses.

3

La alergia a alimentos con omalizumab es menos alergia.

Omalizumab for the Treatment of Multiple Food Allergies.

Robert A Wood, Alkis Togias, Scott H Sicherer, Wayne G Shreffler, Edwin H Kim, Stacie M Jones et al.

N Engl J Med . 2024 Mar 7;390(10):889-899. doi: 10.1056/NEJMoa2312382.

BACKGROUND

Food allergies are common and are associated with substantial morbidity; the only approved treatment is oral immunotherapy for peanut allergy.

METHODS

In this trial, we assessed whether omalizumab, a monoclonal anti-IgE antibody, would be effective and safe as monotherapy in patients with multiple food allergies. Persons 1 to 55 years of age who were allergic to peanuts and at least two other trial-specified foods (cashew, milk, egg, walnut, wheat, and hazelnut) were screened. Inclusion required a reaction to a food challenge of 100 mg or less of peanut protein and 300 mg or less of the two other foods. Participants were randomly assigned, in a 2:1 ratio, to receive omalizumab or placebo administered subcutaneously (with the dose based on weight and IgE levels) every 2 to 4 weeks for 16 to 20 weeks, after which the challenges were repeated. The primary end point was ingestion of peanut protein in a single dose of 600 mg or more without dose-limiting symptoms. The three key secondary end points were the consumption of cashew, of milk, and of egg in single doses of at least 1000 mg each without dose-limiting symptoms. The first 60 participants (59 of whom were children or adolescents) who completed this first stage were enrolled in a 24-week open-label extension.

RESULTS

Of the 462 persons who were screened, 180 underwent randomization. The analysis population consisted of the 177 children and adolescents (1 to 17 years of age). A total of 79 of the 118 participants (67%) receiving omalizumab met the primary end-point criteria, as compared with 4 of the 59 participants (7%) receiving placebo (P<0.001). Results for the key secondary end points were consistent with those of the primary end point (cashew, 41% vs. 3%; milk, 66% vs. 10%; egg, 67% vs. 0%; P<0.001 for all comparisons). Safety end points did not differ between the groups, aside from more injection-site reactions in the omalizumab group.

CONCLUSIONS

In persons as young as 1 year of age with multiple food allergies, omalizumab treatment for 16 weeks was superior to placebo in increasing the reaction threshold for peanut and other common food allergens. (Funded by the National Institute of Allergy and Infectious Diseases and others; ClinicalTrials.gov number, NCT03881696.).

4

4=52: la efectividad a largo plazo de ITA intralinfática es comparable a ITSC.

The long-term efficacy of intra-cervical lymphatic immunotherapy on adults with allergic rhinitis: A randomized controlled study.

Yang Qin, Weijun Huang, Rui Zheng, Qixing Wang, Qingqing Yu, Yin Li et al.

Clin Transl Allergy. 2024 Feb;14(2):e12341.doi: 10.1002/clt2.12341.

BACKGROUND

The efficacy and safety of the novel immunotherapy method, intra-cervical lymphatic immunotherapy (ICLIT), need to be investigated. Comparing it with subcutaneous immunotherapy (SCIT), we clarified the long-term efficacy and safety of intra-cervical lymphatic immunotherapy on allergic rhinitis (AR) and investigated the improvement of clinical efficacy of the booster injection at 1 year after ICLIT treatment.

METHODS

Ninety adult patients with dust mite allergy were randomly divided into 3 groups: 30 in the SCIT group, 30 in the ICLIT group, and 30 in ICLIT booster group. Changes in total symptom score (TSS), nasal symptom score (TNSS), ocular symptom score (TOSS) and total medication score (TMS) were evaluated in the three groups. Adverse reactions were recorded, and serum dust mite specific IgE (sIgE) and specific IgG4 were assessed in the ICLIT group and ICLIT booster group.

RESULTS

TSS, TNSS, TOSS, and TMS scores were significantly lower in the three groups at 36 months after treatment ($p < 0.05$). And at 36 months the ICLITbooster group showed results similar to SCIT and superior to ICLIT ($p < 0.05$). Serum specific IgE decreased in all three groups at 12 and 36 months after treatment, $p < 0.01$. The ICLIT group and the ICLIT booster group showed a significant increase in sIgG4, $p < 0.01$. None of the patients in the three groups had any serious systemic adverse effects during the 3-year follow-up.

CONCLUSION

The ICLIT treatment is effective and safe on AR. One booster injection of allergens at 1 year can greatly improve its long-term efficacy.

5

10 años de seguimiento confirman que la ITA es coste-efectiva.

Long-term health care resource and cost savings with allergy immunotherapy: REACT study results.

Benedikt Fritzsching, Celeste Porsbjerg, Marco Contoli, Sarah Buchs, Julie Rask Larsen, Nick Freemantle

J Allergy Clin Immunol Glob. 2023 Nov 23;3(1):100197. doi: 10.1016/j.jacig.2023.100197. eCollection 2024 Feb.

BACKGROUND

Allergy immunotherapy (AIT) can be administered as subcutaneous immunotherapy (SCIT) injections in the clinic or as sublingual immunotherapy (SLIT) tablets at home after initiation under medical supervision. To achieve long-term, sustained effects, a 3-year treatment duration is recommended.

OBJECTIVE

Our aim was to assess the association of AIT (SCIT and SLIT tablets) with long-term health care resource use (HRU) and costs in subjects with allergic rhinitis.

METHODS

REACT was a retrospective propensity score matched cohort study using claims data from a German health insurance database (2007-2017), with up to 9 years of follow-up after AIT initiation. HRU and costswere evaluated for hospitalizations, ambulatory care visits, and prescriptions, in subjects who received AIT versus in matched controls with allergic rhinitis who had not received AIT, as well as for SCIT and SLIT tablets.

RESULTS

Across all 9 years, the subjects who received AIT had a significantly lower incidence of hospitalization than the controls did. Generally, proportions of subjects with ambulatory care visits and hospitalizations were lower, and length of hospitalization was shorter, for those receiving SLIT tablets than those who received SCIT. Total costs were significantly higher with AIT versus for the controls during the treatment period (years 1 to 3), driven by prescriptions and ambulatory care visits, but they were lower in years 4 to 9. During years 1 to 3, prescription costs were generally higher for SLIT tablets than for SCIT, whereas ambulatory care costs were numerically lower. In most years, hospitalization costs were numerically lower for SLIT tablets than for SCIT.

CONCLUSION

Initial higher HRU and costs of AIT during the expected treatment period are offset in the long term. At home administration of SLIT tablets may further reduce ambulatory care costs.

6

ITO con cacahuete, ¿mejor rápida y mucha dosis o lenta y poca?

High degree of desensitization after one year of early-life peanut oral immunotherapy - SmaChO Randomized Controlled Trial.

Carina Uhl, Susanna Klevebro, Eva Sverremark-Ekström, Sandra G Tedner, Josef Brandström, Chrystalleni Papageorgiou et al

J Allergy Clin Immunol Pract. 2024 Feb 28:S2213-2198(24)00204-6. doi: 0.1016/j.jaip.2024.02.030. Online ahead of print.

BACKGROUND

The prevalence of peanut allergy is about 2% and mostly lifelong. Studies of oral immunotherapy (OIT) with peanut - daily oral intake of an initially low and then increasing dose of peanut - often show problematic side effects but there are indications of better safety and effect in younger children compared with older children and adults.

OBJECTIVE

To determine the safety and effectiveness of peanut OIT with a slow up-dosing strategy and low maintenance dose, in peanut allergic children 1-3 years of age, a 1-year interim analysis.

METHODS

In a randomized controlled trial (2:1 ratio) 75 children with median age 31 months (IQR 23 - 40) were assigned to receive peanut oral immunotherapy (OIT) (n=50) or peanut avoidance (n=25).

RESULTS

In the OIT group and the avoidance group, 43/50 and 20/25 children, respectively, performed the 1-year open oral peanut challenge. A cumulative dose of 750 mg peanut protein after one year was tolerated by 72% (36/50) in the OIT-group compared to 4% (1/25) in the avoidance-group, $p<0.001$. Median tolerated cumulative dose was 2750 mg (IQR 275 - 5000) peanut protein in the OIT-group compared to 2.8 mg (IQR 0.3 - 27.8) in the avoidance-group, $p<0.001$. Of the doses administered at home during the first year of OIT, 1.4% resulted in adverse events, 79% were mild, and three doses of epinephrine were given at home to two individuals.

CONCLUSION

In children 1-3 years of age, peanut OIT with the combination of slow up-dosing and low maintenance dose seems safe and effective after one year.

7

IT epicutánea con leche, sí entre 2-11 años.

Varying Doses of Epicutaneous Immunotherapy With Viaskin Milk vs Placebo in Children With Cow's Milk Allergy : A Randomized Clinical Trial.

Daniel Petroni, Philippe Bégin, J Andrew Bird, Terri Brown-Whitehorn, Hey J Chong, David M Fleischer et al.

JAMA Pediatr. 2024 Feb 26:e236630. doi: 10.1001/jamapediatrics.2023.6630.

IMPORTANCE

No approved treatment exists for allergen specific immunoglobulin E (IgE)-mediated cow's milk allergy (CMA), a common childhood food allergy.

OBJECTIVE

To assess dose, efficacy, and safety of epicutaneous immunotherapy with Viaskin milk in children with IgE-mediated CMA.

DESIGN, SETTING, AND PARTICIPANTS

A phase 1/2, 2-part, randomized, double-blind, placebo-controlled dose ranging clinical trial in children aged 2 to 17 years with IgE-mediated CMA was conducted between November 2014 through December 2017. It took place at 17 trial sites in the US and Canada. Current CMA was confirmed by double-blind, placebo-controlled food challenge at study entry. Part A assessed the short-term safety of 150 μg, 300 μg, or 500 μg of Viaskin milk; part B evaluated the efficacy and safety of the 3 doses vs placebo over 12 months of treatment. Of the 308 screened participants with physician-diagnosed CMA, 198 met eligibility criteria (including an eliciting dose 300 mg or less) and were randomized.

INTERVENTIONS

Safety of Viaskin milk (150-μg, 300-μg, or 500-μg doses) was evaluated over a 3-week period (part A). In part B, 180 additional participants were randomized to receive Viaskin milk at doses of 150 μg, 300 μg, or 500 μg or placebo (1:1:1:1) for 12 months.

MAIN OUTCOMES AND MEASURES

The primary outcome was the proportion of treatment responders, defined as a 10 fold or more increase in the cumulative reactive dose of cow's milk protein (reaching at least 144 mg) or a cumulative reactive dose of cow's milk protein at 1444 mg or more at the month 12 double-blind, placebo-controlled food challenge.

RESULTS

A total of 95.5% of the randomized participants (mean [SD] age, 8 [4.17] years; 124 of 198 were male [62.6%]) completed treatment. The highest response rate was observed in participants who received Viaskin milk at the 300-μg dose with 24 of 49 responders (49.0%) overall vs 16 of 53 responders (30.2%) in the placebo group (odds ratio, 2.19; 95% CI, 0.91-5.41; P = .09), highest in the 2 to 11 years age group (22 of 38 [57.9%] vs 13 of 40 [32.5%]; P = .04). Most treatment-emergent adverse events were mild or moderate application-site reactions. One participant in the 500-μg Viaskin milk dose group experienced treatment-related anaphylaxis.

CONCLUSIONS AND RELEVANCE

In this randomized clinical trial, 12 months of daily epicutaneous immunotherapy with a dose of Viaskin milk at 300 μg was associated with a statistically significant treatment response in 2- to 11-year-old children with IgE-mediated CMA. Treatment-related anaphylaxis and treatmentrelated discontinuation rates were low. Further research is needed to explore Viaskin milk as a viable treatment option for children with IgE-mediated CMA.

8

Alérgico a abeja pero ... ¿a qué alérgeno? Conoce tu riesgo.

Molecular profiling in bee venom allergy: clinical and therapeutic characterization in a Portuguese cohort.

Cardoso Lopes, P Botelho Alves, H Pires Pereira F Cunha, I Farinha, A Maresch et al.

Eur Ann Allergy Clin Immunol. 2024 Feb 20. doi: 10.23822/EurAnnACI.1764-1489.332.

BACKGROUND

Bee venom allergy (BVA) can trigger local and systemic allergic reactions, including anaphylaxis. Recently, the molecular sensitization profile has gained importance in the reaction's stratification and venom immunotherapy (VIT).

METHODS

Retrospective analysis of patients with hypersensitivity to BVA, confirmed by specific sIgE to Apis mellifera ≥0.35 kU/L and/or positive skin tests to bee venom commercial extract, evaluated in specialized consultation. Demographic, clinical, and laboratory data (including molecular Api m 1, 4, and 10) were analyzed, looking for risk factors associated with the severity of the index reaction and reactions during VIT.

RESULTS

93 patients were included (55.9% male; median age of 46 years), 57.3% with atopic comorbidities, and 23.4% with cardiovascular comorbidities. The median specific IgE to Apis mellifera was 6.7 kU/L (IQR 1.0-20.3) kU/L. Regarding the molecular profile, the median IgE to Api m 1 was 0.5 kU/L (57.5% positive out of all measurements); Api m 4 - 0.01 kU/L (11.9% positive), and Api m 10 - 0.3 kU/L (50.0% positive). No patient was monosensitized to Api m 4. The median age of the most severe sting reaction was 36 (IQR 26-48) years, with a median severity (Müeller scale) of 3 (IQR 2-3). Forty-seven patients (50.5%) underwent VIT, with 35.6% of reactions recorded. Allergic reactions during VIT were recorded in 35.6% of cases. The severity of the index reaction correlated positively with older ages (p=0.040; r=0.249), in contrast to monosensitization to Api m 1, which was an independent predictor of milder reactions (p=0.015). Sensitization to Api m 10 was associated with a higher likelihood of reactions during VIT (p=0.038) but potentially less systemic reactions at re-stings (p=0.097).

CONCLUSIONS

Molecular sensitization profile appears to be relevant not only to the severity of index reactions but also during VIT. Studies of a large cohort of patients with molecular profiles are essential to validate these results and improve the clinical and therapeutic approach to BVA.

9

¿Cuánto es suficiente en ITO con leche?

Low-dose oral immunotherapy in immunoglobulin E-mediated food allergies.

Dongxia Ma, Rongfei Zhu

Front Immunol. 2024 Feb 1:15:1321863. doi: 10.3389/fimmu.2024.1321863.

ABSTRACT

Nowadays, the management of food allergies has increasingly moved from conventional oral immunotherapy (OIT) to low-dose OIT or low-dose OIT utilizing hypoallergenic foods. This shift is largely because the latter appears to induce oral tolerance with fewer adverse effects than the former. However, the mechanisms underpinning such differences remain unclear. To better understand these mechanisms, we conducted a comparative study scrutinizing the mechanisms of OIT, especially those of low-dose desensitization. We also summarized articles on low-dose OIT and low-dose OIT using hypoallergenic foods. We examined the efficacy, safety, and immunological parameters of low dose OIT and those of low-dose OIT with hypoallergenic foods with the aim of shedding some light on lowdose OIT and its therapeutic application in inducing oral tolerance for individuals with food allergies.

10

Mejores ITAs frente a nuestras mascotas evitarán “expulsiones forzosas”.

Why is Pet (cat/dog) allergen immunotherapy (ait) such a controversial topic? current perspectives and future directions.

G Liccardi, M Martini, M B Bilò, L Cecchi, M Milanese, L Brussino et al.

Eur Ann Allergy Clin Immunol. 2024 Feb 13. doi: 10.23822/EurAnnACI.1764-1489.330.

ABSTRACT

Dogs and cats are the most common pets worldwide. In Italy, the prevalence of allergic sensitization to cats and dogs is 16% and 9% respectively. The limited standardization of allergenic extracts, especially for dogs, emphasizes the importance of Component Resolved Diagnosis (CRD) for accurate diagnosis and subsequent prescription of allergen immunotherapy (AIT). However, this low standardization is the main factor contributing to the unsatisfactory clinical efficacy of traditional AIT, AIT with modified allergens, and intralymphatic allergen-specific immunotherapy (ILAIT). Emerging immunological approaches, particularly for controlling the primary cat allergen, show promise but are hindered by high costs (e.g., use of anti-Fel d 1 monoclonal antibodies in humans) or by exclusively targeting Fel d 1 produced by one's own animal (e.g., immunizing cats to induce neutralizing antibodies against Fel d 1 or including an egg product with anti Fel d 1 IgY antibodies in feline diet). Further studies are imperative for standardizing pet allergens, enhancing the efficacy of various AIT modalities, and exploring other immunological approaches, to optimize the relationship between pets and their owners and prevent distressing "forced removals".

BBI BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Marzo 2024

1

¿Anafilaxia por himenópteros? Sospecha enfermedad mastocitaria.

High burden of clonal mast cell disorders and hereditary α-tryptasemia in patients who need Hymenoptera venom immunotherapy.

Korošec P, Sturm GJ, Lyons JJ, Marolt TP, Svetina M, et al

Allergy. 2024 Mar 13. Epub ahead of print. PMID: 38477502.

BACKGROUND

In patients who require venom immunotherapy (VIT), there is a need to identify underlying mast cell (MC) disorders since these may affect the risk and severity of future sting reactions and the long-term effectiveness of VIT.

METHODS

1319 individuals with Hymenoptera venom allergy (HVA) who needed VIT from referral centers in Slovenia, Austria, Croatia, and Poland underwent examination for KIT p.D816V in peripheral blood leukocytes (PBL) using a highly sensitive PCR test and tryptase genotyping by digital droplet PCR. We also included 183 control individuals with large local reactions (LLRs) to Hymenoptera stings and with asymptomatic sensitization to Hymenoptera venoms.

RESULTS

285 of 1319 individuals recommended for VIT (21.6%) were positive for KIT p.D816V in PBL, preferably those who present with severe reaction (33.9% [n = 207 of 610] with Ring Messmer grade 3-4 vs. 11% [n = 78 of 709] with Grade 1 2; p < .0001), whereas only 1.3% (n = 2 of 152) of controls with LLR and none with asymptomatic sensitization (n = 31) had KIT p.D816V. KIT p.D816V allelic burden was higher in those with severe reaction (median 0.018% [n = 207] in Grade 3-4 vs. 0.001% [n = 78] in Grade 1-2; p < .0001), and the majority had normal baseline serum tryptase levels (69% [n = 196 of 285]). All KIT p.D816V-positive individuals (n = 41) who underwent bone marrow (BM) biopsy were found to have underlying clonal diseases, principally BM mastocytosis. HαT was also associated with severe HVA and symptoms (p < .01), and remarkably, 31.0% (n = 31 of 100) were found to have concomitant KIT p.D816V. Concomitant HαT and KIT p.D816V showed an additive effect, and having both was associated with the highest risk for severe HVA, even higher than having either HαT or KIT p.D816V alone (OR = 3.8; p < .01).

CONCLUSIONS

By employing prospective universal tryptase genotyping and examination for KIT p.D816V in PBL in large HVA populations, we have demonstrated a high burden of clonal MC disorders and HαT in patients who require VIT.

2

En la rinitis alérgica local crear anticuerpos bloqueantes predice la respuesta a ITA.

Nasal allergen-neutralizing antibodies correlate closely with tolerated intranasal allergen challenge dose following grass pollen subcutaneous immunotherapy in patients with local allergic rhinitis.

Eguiluz-Gracia I, Parkin RV, Layhadi JA, Palmer E, Meng X, et al

Allergy. 2024 Mar 14. Epub ahead of print. PMID: 38483174.

BACKGROUND

Local allergic rhinitis (LAR) is defined by chronic nasal symptoms, absence of atopy, positive nasal allergen challenge (NAC) and a good response to subcutaneous allergen immunotherapy (SCIT). We sought to investigate SCIT capacity to induce local and systemic blocking antibodies in LAR patients.

METHODS

A RDBPC study of grass SCIT was performed, with participants receiving either SCIT (Group A; n = 10) or placebo (Group B; n = 14) in the first 6 months. Both groups subsequently received SCIT for 12 months at Year 2. Nasal and serum antibodies (IgG4 , IgA1 and IgA2) and their inhibitory capacity were measured at multiple timepoints.

RESULTS

The allergen concentration tolerated increased significantly at 6 months (Group A; p = .047) and 24 months (Group B; p = .049) compared with baseline and persisted until the end of the study. Induction of serum sIgA1 to Phl p was seen in Groups A and B, albeit the former being induced earlier (1.71-fold, p = .027). A significant induction in sIgG4 to Phl p 1 and 5 was observed in serum of Group A (p = .047 and p = .0039) and sIgA2 to Phl p in Group B (p = .032 and p = .0098) at 18 and 24 months, respectively. Both local and systemic blocking antibodies can inhibit allergen-IgE complexes binding to CD23 on B cells, and this correlated with level of allergen tolerated intranasally in Group A (serum; ρ = -.47, p = .0006, nasal; ρ = -.38, p = .0294).

CONCLUSIONS

Grass pollen SCIT induced functional systemic blocking antibodies that correlate with the concentration of allergen tolerated following NAC, highlighting their potential as a biomarker of SCIT in LAR.

3

Ciclofilina, un panalergeno “desconocido”.

IgE to cyclophilins in pollen allergic children: epidemiological, clinical and diagnostic relevance of a neglected panallergen.

Matricardi PM, Potapova E, Panetta V, Lidholm J, Mattsson L et al, Italian Pediatric Allergy Network

J Allergy Clin Immunol. 2024 Mar 19:S0091-6749(24)00235-5. Epub ahead of print. PMID: 38513837.

BACKGROUND

Cyclophilins are ubiquitous panallergens whose epidemiological, diagnostic, and clinical relevance is largely unknown and whose sensitization is rarely examined in routine allergy practice. The aim of this study was to investigate the epidemiological, diagnostic, and clinical relevance of cyclophilin in seasonal allergic rhinitis and its comorbidities.

METHODS

We examined a random sample (25%, n 253) of 1263 Italian children affected by seasonal allergic rhinitis from the "Panallergen in Pediatrics" (PANPED) cohort. Patients' disease phenotype had been already fully characterized through questionnaires (ARIA), skin prick tests (ALK), IgE tests to extracts, major and cross-reactive allergenic molecules of a comprehensive variety of allergenic pollen (immunoCAP), and carbohydrate cross-reacting determinants (CCD) (NOVEOS). We also performed nested studies of sensitization prevalence, correlation and allergen extract inhibition in patients (A) sensitized to birch pollen extract but lacking IgE to Bet v 1, Bet v 2, and Bet v 4, (74/1263) or with the highest serum level of IgE to Bet v 1 (26 within 1263), and (B) in patients with sensitization to extracts of ragweed (18), mugwort (18), pellitory (20), Plantago (19), and plane tree (20), but not to their respective major allergenic molecule, profilins and polcalcins. IgE to cyclophilin was detected with recombinant Bet v 7 (ImmunoCAP) and extract inhibition tests were performed with the same rBet v 7.

RESULTS

In the randomized population, IgE to rBet v 7 was detected in 43/253 (17%) patients. It was associated with asthma ($p<0.028$) and oral allergy syndrome ($p<0.017$) in univariate, but not in a multivariate analysis adjusted for IgE to profilins (Phl p 12), PR.10s (Bet v 1), and LTPs (Pru p 3). IgE to r Bet v 7 was also highly prevalent (47/74; 63%) among patients with unexplained sensitization to birch pollen extract. In patients with unexplained sensitization to ragweed, mugwort, pellitory, Plantago and plane tree pollen, the levels of IgE to those extracts correlated with the levels of IgE to rBet v 7, and they were also significantly inhibited by rBet v 7 (inhibition range 45%- 74%).

CONCLUSIONS

IgE sensitization to cyclophilin is very frequent in pollen allergic patients living in temperate areas and can produce “false” positive outcomes in SPT and IgE tests to many different pollen extracts. The spectrum of pollen species containing allergenic cyclophilins is probably broader than previously known. Our results suggest that guidelines of molecular diagnostics should include this allergen family and that new tests based on plant cyclophilins should be produced and used with sera of pollen-allergic patients for a more precise identification of the culprit pollen extract and a tailored prescription of allergen immunotherapy.

4

Resultados en “vida real” sobre la efectividad a largo plazo de la ITA.

House dust mite SCIT reduces asthma risk and significantly improves long-term rhinitis and asthma control-A RWE study.

Jutel M, Klimek L, Richter H, Brüggenjürgen B, Vogelberg C

Allergy. 2024 Apr;79(4):1042-1051. Epub 2024 Mar 2. PMID: 38429981.

BACKGROUND

The German Therapy Allergen Ordinance (TAO) triggered an ongoing upheaval in the market for house dust mite (HDM) allergen immunotherapy (AIT) products. Three HDM subcutaneous AIT (SCIT) products hold approval in Germany and therefore will be available after the scheduled completion of the TAO procedure in 2026. In general, data from clinical trials on the long-term effectiveness of HDM AIT are rare. We evaluated real-world data (RWD) in a retrospective, observational cohort study based on a longitudinal claims database including 60% of all German statutory healthcare prescriptions to show the long-term effectiveness of one of these products in daily life. Aim of this analysis was to provide a per product analysis on effectiveness of mite AIT as it is demanded by international guidelines on AIT.

METHODS

Subjects between 5 and 70 years receiving their first (index) prescription of SCIT with a native HDM product (SCIT group) between 2009 and 2013 were included. The exactly 3:1 matched control group received prescriptions for only symptomatic AR medication (non-AIT group); the evaluation period for up to 6 years of follow-up ended in February 2017. Study endpoints were the progression of allergic rhinitis (AR) and asthma, asthma occurrence and time to the onset of asthma after at least 2 treatment years.

RESULTS

In total, 892 subjects (608 adults and 284 children/adolescents) were included in the SCIT group and 2676 subjects (1824 adults and 852 children/adolescents) in the non-AIT group. During the follow-up period after at least 2 years of SCIT, the number of prescriptions in the SCIT group was reduced by 62.8% ($p < .0001$) for AR medication and by 42.4% for asthma medication ($p = .0003$). New-onset asthma risk was significantly reduced in the SCIT vs non-AIT group by 27.0% ($p = .0212$). The asthma-preventive effect of SCIT occurred 15 months after start of the treatment. In the SCIT group, the time to onset of asthma was prolonged compared to the non-AIT group ($p = .0010$).

CONCLUSION

In this first product based RWD analysis on SCIT with a native HDM product, patients aged 5 to 70 years benefited from AIT in the long term in terms of reduced progression of AR and asthma after at least 2 years of treatment. The effects seemed to last for up to 6 years after treatment termination. A significantly reduced risk of asthma onset was observed, starting after 15 months of treatment.

5

La IT epicutánea con cacahuete analizada con lupa.

From Skin to Solution: Exploring Epicutaneous Immunotherapy for Peanut Allergy-A Systematic Review and Meta-Analysis.

Banatwala UESS, Nasir MM, Javed R, Ahmed A, Farhan SA, Ajam A

Clin Rev Allergy Immunol. 2024 Mar 25. Epub ahead of print. PMID: 38526693.

ABSTRACT

Peanut allergy is a leading cause of severe food reactions. This meta-analysis evaluates the efficacy and safety of epicutaneous immunotherapy (EPIT) compared to placebo for peanut allergic individuals. After prospectively registering on PROSPERO, we searched three databases (PubMed, Google Scholar, and Cochrane CENTRAL) and 2 trial registries till September 2023. Analysis was conducted via RevMan where data was computed using risk ratios (RR). The Cochrane Risk of Bias tool and GRADE criteria were used to appraise and evaluate the evidence. From 4927 records, six multicenter randomized placebo-controlled trials comprising 1453 participants were included. The 250 µg EPIT group had a significant increase in successful desensitization compared to placebo (RR: 2.13 (95% C.I: 1.72, 2.64), P < 0.01, I2 = 0%), while the 100 µg EPIT group did not (RR: 1.54 (95% C.I: 0.92, 2.58), P = 0.10, I2 = 0%) (moderate certainty evidence). Moreover, there was a significant increase in local (RR: 1.69 (95% C.I: 1.06, 2.68), P = 0.03, I2 = 89%) and systemic adverse events (RR: 1.75 (95% C.I: 1.14, 2.69), P = 0.01, I2 = 0%) with EPIT. Additionally, individuals administered EPIT have an increased probability of requiring rescue medications like epinephrine (RR: 1.91 (95% C.I: 1.12, 3.28), P = 0.02, I2 = 0%) and topical corticosteroids (RR: 1.49 (95% C.I: 1.29, 1.73), P < 0.01, I2 = 0%) to treat adverse events. The association of adverse events post-treatment including anaphylaxis (RR: 2.31 (95% C.I: 1.00, 5.33), P = 0.05, I2 = 36%), skin/subcutaneous disorders like erythema or vesicles (RR: 0.93 (95% C.I: 0.79, 1.08), P = 0.33, I2 = 0%), and respiratory disorders like dyspnea or wheezing (RR: 0.94 (95% C.I: 0.77, 1.15), P = 0.55, I2 = 0%) with EPIT is inconclusive. EPIT, although effective in desensitization, is linked to an increased risk of adverse events. PROSPERO registration: CRD42023466600.

6

Enfoque por terciles para calcular mejor la efectividad de la ITA.

Efficacy of 300 IR house dust mite immunotherapy as a function of disease activity: Tertile analysis in clinical trials.

Devillier P, Demoly P, Gentil C, Bergmann KC, Casale TB, Okamoto Y, Pfaar O

Clin Exp Allergy. 2024 Mar 28. Epub ahead of print. PMID: 38545699.

BACKGROUND

The symptoms of house dust mite (HDM) induced allergic rhinitis (AR) vary with changes in exposure related to the weather or the domestic environment. In allergen immunotherapy (AIT) studies, a certain level of AR disease activity is necessary to demonstrate treatment efficacy; the latter can be underestimated if a substantial proportion of the patient population is weakly symptomatic.

OBJECTIVE

To better estimate the real treatment effect of a HDM sublingual AIT (SLIT) tablet, we analysed the results of natural field studies in detail by applying a tertile approach.

METHODS

We used data from three randomised, controlled trials (RCT) in a total of 2585 patients with AR treated with the 300 index of reactivity (IR) HDM SLIT-tablet or placebo. The study centres were grouped into tertiles according to the level of combined symptom and medication scores in patients in the placebo group. In each tertile, the difference between SLIT and placebo was assessed through an analysis of covariance.

RESULTS

In the three RCTs, combined scores were found to be similar in the SLIT and placebo groups in the low tertiles. The treatment effect of the 300 IR HDM tablet increased in the medium and high tertiles, with notably significant differences versus placebo in the highest tertile and greater (ranging from -21% to -39%) than in the entire study population (-13% to -20%). The positive relationship between treatment efficacy and the combined score in each tertile was independent of the RCT and the score used.

CONCLUSIONS AND RELEVANCE

Application of the tertile approach to AIT studies in a field in which many variables interact strongly might provide more accurate and meaningful measurements of efficacy and benefit for patients, better reflecting their real-life condition.

7

Efectividad de la ITO medido desde la transcriptómica.

Transcriptomic changes associated with oral immunotherapy for food allergy.

Ashley SE, Bosco A, Tang MLK

Pediatr Allergy Immunol. 2024 Mar;35(3):e14106. PMID: 38520061.

ABSTRACT

This review summarizes recent advances in characterizing the transcriptional pathways associated with outcomes following Oral Immunotherapy. Recent technological advances including single-cell sequencing are transforming the ways in which the transcriptional landscape is understood. The application of these technologies is still in its infancy in food allergy but here we summarize current understanding of gene expression changes following oral immunotherapy for food allergy and specific signatures underpinning the different clinical outcomes of desensitization and remission (sustained unresponsiveness). T helper 2A cells have been identified as a cell type which correlates with disease activity and is modified by treatment. Molecular features at study entry may differentiate individuals who achieve more positive outcomes during OIT. Recent findings point to T cell anergy and Type 1 interferon pathways as potential mechanisms supporting redirection of the allergen specific immune response away from allergy towards remission. Despite these developments in our understanding of immune mechanisms following OIT, there are still significant gaps. Additional studies examining immune signatures associated with long term and well defined clinical outcomes are required to gain a more complete understanding of the pathways leading to remission of allergy, in order to optimize treatments and gain improved outcomes for patients.

8

Evidencia de la efectividad a largo plazo de los comprimidos en niños.

SQ sublingual immunotherapy tablets for children with allergic rhinitis: A review of phase three trials.

Csonka P, Hamelmann E, Turkalj M, Roberts G, Mack DP

Acta Paediatr. 2024 Mar 26. Epub ahead of print. PMID: 38529710.

AIM

To provide paediatricians with a summary of efficacy and safety of SQ sublingual immunotherapy (SLIT) tablets from phase three, randomised, double-blind, placebo-controlled trials in children and adolescents with allergic rhinitis or rhinoconjunctivitis, with and without asthma.

METHODS

PubMed searches were conducted and unpublished data were included if necessary.

RESULTS

Of the 93 publications, 12 were identified reporting 10 trials. One trial was excluded as paediatric specific efficacy data were unavailable. The nine eligible trials evaluated grass, house dust mite, ragweed and tree SLIT tablets. Consistent reductions in allergic rhinitis or rhinoconjunctivitis symptoms and medication use were observed with SQ SLIT tablets versus placebo. In a five-year trial, sustained reduction of allergic rhinoconjunctivitis symptoms, asthma symptoms and medication use were observed with SQ grass SLIT tablet versus placebo. The number-needed-to-treat to prevent asthma symptoms and medication use in one additional child during follow-up was lowest in younger children. SQ SLIT tablets were generally well tolerated across trials.

CONCLUSION

Evidence supports use of SQ SLIT tablets in children and adolescents with allergic rhinitis or rhinoconjunctivitis, with and without asthma. Long-term data demonstrate disease modifying effects of SQ grass SLIT tablet and suggest the clinical relevance of initiating allergy immunotherapy earlier in the disease course.

9

El uso de Apps durante la ITO mejora el cumplimiento y el manejo de incidencias.

Mobile App/Web Platform for Monitoring Food Oral Immunotherapy in Children: Longitudinal Clinical Validation Study.

Sánchez-Fernández S, Lasa EM, Terrados S, Sola-Martínez FJ, Martínez-Molina S, López de Calle M, Cabrera-Freitag P, Goikoetxea MJ

JMIR Pediatr Parent. 2024 Mar 13;7:e54163. PMID: 38477961; PMCID: PMC10973957.

BACKGROUND

Milk and egg allergies significantly impact the quality of life, particularly in children. In this regard, food oral immunotherapy (OIT) has emerged as an effective treatment option; however, the occurrence of frequent adverse reactions poses a challenge, necessitating close monitoring during treatment.

OBJECTIVE

This study aims to evaluate the ability of a new mobile/web app called OITcontrol to monitor milk and egg OIT.

METHODS

Patients undergoing milk or egg OIT were recruited and divided into 2 groups: the active group used the OITcontrol app in conjunction with standard written monitoring methods, whereas the control group relied solely on written diaries. Investigators documented hospital doses, hospital reactions, and administered treatments on the website. Patients recorded their daily allergen homedose intake, home reactions, and administered treatments using the app. The following variables were compared between both groups: number and severity of hospital and reported home reactions, patient's adhesion to the OITcontrol app or written diary or both in terms of daily home-dose intake and home reactions recording, and treatment and dose adjustment compliance at home in case of reaction.

RESULTS

Sixteen patients were assigned to be monitored using the OITcontrol app along with additional written methods (active group), while 14 patients relied solely on a written paper diary (control group). A similar distribution was observed in terms of sex, age, basal characteristics, allergen treated in OIT, premedication, and sensitization profile. Active patients reported a comparable number of hospital and home reactions compared with the control group. In terms of recording system usage, 13/16 (81%) active patients used the OITcontrol app, while 10/14 (71%) control patients relied on the written diary. Among active patients, 6/16 (38%) used both methods, and 1 active patient used only written methods. However, control patients recorded home reactions more frequently than active patients (P=.009). Among active patients, the app was the preferred method for recording reactions (59/86, 69%), compared with the written diary (15/86, 17%) or both methods (12/86, 14%; P<.001). Treatment compliance in home-recorded reactions was similar between both groups (P=.15). However, treatment indications after an adverse reaction were more frequently followed (P=.04) in reactions recorded solely in the app (36/59, 61%) than in the written diary (29/71, 41%) or both systems (4/12, 33%). Moreover, compliance with dose adjustments after a moderate-severe reaction in home-recorded reactions was higher in the active group than in the control group (P<.001). Home reactions recorded only in the app (16/19, 84%) were more likely to follow dose adjustments (P<.001) than those recorded in the written diary (3/20, 15%) or using both methods (2/3, 67%).

CONCLUSIONS

The OITcontrol app appears to be a valuable tool for monitoring OIT treatment in children with food allergies. It proves to be a suitable method for recording daily home dose intakes and reactions, and it seems to enhance adherence to treatment indications following an adverse reaction as well as compliance with dose adjustments in home reactions. However, additional studies are necessary to comprehensively grasp the benefits and limitations of using the OITcontrol app in the management of OIT.

10

La importancia de los adyuvantes en ITO.

Purified Free Mannan Promotes Tolerogenic Responses in Peanut-Stimulated Human Dendritic Cells.

Sánchez-Herrero S, Benito-Villalvilla C, Palomares O

Int Arch Allergy Immunol. 2024 Mar 21:1-7. doi: 10.1159/000537989. Epub ahead of print. PMID: 38513626.

INTRODUCTION

IgE-mediated peanut allergy is an important public health problem of increasing prevalence leading to anaphylactic reactions both in children and adults. Allergen-specific oral immunotherapy (OIT) is the single treatment with the potential capacity to modify the course of the disease, but it still faces some drawbacks in terms of efficacy, safety, patients' adherence, and cost. Alternative strategies, including the use of novel adjuvants, to overcome such limitations are highly demanded. The main aim of this study was to search for potential novel adjuvants for peanut OIT by assessing the capacity of free purified mannan and different toll-like receptor ligands (TLR-Ls) to immunomodulate the responses of human monocyte-derived dendritic cells (hmoDCs) to peanut allergens.

METHODS

Monocytes were isolated from PBMCs of healthy donors and differentiated into hmoDCs. Flow cytometry, ELISA, coculture, and suppression assay were performed to assess the effects of TLR-Ls, mannan, and crude peanut extract (CPE) in hmoDCs.

RESULTS

Purified free mannan increased the expression levels of HLA-DR, CD86, CD83, and PD-L1 and induced a higher IL-10/IL-6 cytokine ratio in hmoDCs compared to the stimulation with different TLR-Ls. Mannan significantly increased the expression of HLA-DR, the maturation marker CD83, the tolerogenic marker PD-L1, as well as the production of IL-10, IL-6, and TNF-α in CPE stimulated hmoDCs. Supporting these tolerogenic properties, mannan also significantly increased the frequency of FOXP3+ regulatory T cells generated by CPE-treated hmoDCs with functional suppressive capacity.

CONCLUSIONS

We uncover that purified free mannan induces tolerogenic responses in human DCs stimulated with peanut allergens, suggesting mannan as a suitable potential novel adjuvant to be exploited in the context of OIT for peanut allergy.

BOLETÍN BIBLIOGRÁFICO
DE INMUNOTERAPIA

Abril 2024

1

Análisis sobre el ABC de la inmunoterapia

Allergen Immunotherapy: The Evidence Supporting the Efficacy and Safety of Subcutaneous Immunotherapy and Sublingual Forms of Immunotherapy for Allergic Rhinitis/Conjunctivitis and Asthma

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J Allergy Clin Immunol Pract. 2024 Apr 27:S2213-2198(24)00419-7

ABSTRACT

Allergen immunotherapy is a recognized key therapeutic modality for the treatment of allergic respiratory disease -definitive studies have provided evidencebased data to demonstrate its effectiveness in allergic rhinitis and asthma due to the inhalation of proteinaceous allergic substances from specific seasonal pollens, dust mites, animal allergens, and certain mold spores. Over the ensuing decades, laboratory investigations, have provided objective evidence to demonstrate immunologic changes, including production of protective IgG antibody, suppression of IgE antibody, upregulation of regulatory T-cells, and an induction of a state of immune tolerance to the offending allergen(s). Tangential to this work were carefully designed clinical studies that defined allergen dose and duration of treatment, established the importance of preparing extracts with standardized allergens (or well defined extracts) based on major protein moieties, utilized allergen provocation models to demonstrate efficacy superior to placebo. In the U.S., the use of subcutaneous immunotherapy (SCIT) extracts for allergen immunotherapy (AIT) was grandfathered in by the FDA based on expert literature review. In contrast, sublingual tablet immunotherapy (SLIT-tablets) underwent formal clinical development programs (Phase I III clinical trials) that provided the necessary clinical evidence for safety and efficacy that led to regulatory agency approvals for the treatment of allergic rhinitis in properly characterized allergic patients. The allergy specialist's treatment options currently include traditional subcutaneous allergen immunotherapy and specific sublingual tablets approved for grass, ragweed, house dust mites, trees belonging to the birch homologous group, and Japanese Cedar. Tangential to this are sublingual drops (SLIT-drops) that are increasingly being used off-label (albeit not FDAapproved) in the U.S. This article will review the evidence-based literature supporting the use of these forms of AIT, as well as focus on several current controversies and gaps in our knowledge base that have relevance for the appropriate selection of patients for treatment with specific AIT.

2

Búsqueda de dosis óptima en polimerizado de abedul conjugado con manano

A randomized, double-blind, placebo-controlled trial with mannan-conjugated birch pollen allergoids

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Allergy. 2024 Apr;79(4):990-1000

BACKGROUND

There is still great need to develop new strategies to improve the efficacy of allergen immunotherapies with optimal safety standards for patients. A new promising approach is to couple allergoids to mannan. The objective of this phase IIa/IIb study was to identify the optimal dose of mannan-conjugated birch pollen allergoids for the short-course treatment of birch pollen-induced allergic rhinoconjunctivitis.

METHODS

For this prospective, randomized, double-blind, placebo-controlled, dose-finding study, 246 birch pollen allergic adults received 0.5 mL placebo or 1000, 3000 or 10,000 mTU/mL of mannan-conjugated birch pollen allergoids at five pre-seasonal visits. Efficacy was assessed by comparing allergic rhinoconjunctivitis symptoms and use of anti-allergic medication during the peak of the birch pollen season 2020. Immunologic, tolerability and safety effects were also analysed.

RESULTS

The highest dose of mannan-conjugated birch pollen allergoids reduced the combined symptom and medication score during the peak birch pollen season by a median of 24.7% compared to placebo. The production of Bet v 1 specific IgG4 significantly increased in a dose-dependent manner (3.6- and 4.5-fold) in the 3000 and 10,000 mTU/mL groups. The Bet v 1 specific IgE/IgG4 ratio was also strongly reduced (up to -70%). No fatalities nor serious adverse events were reported, and no adrenaline was used. In total, four systemic reactions occurred (two grade I and two grade II).

CONCLUSION

All doses of mannan-conjugated birch pollen allergoids can be considered as safe. Since the application of 10,000 mTU/mL resulted in the highest efficacy, this dose qualifies for further investigation.

3

Los alergoides con tirosina son efectivos hasta 10 años después de su administración

Long-term effects of pollen allergoid tyrosine-adsorbed subcutaneous immunotherapy on allergic rhinitis and asthma

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Clin Exp Allergy. 2024 Apr;54(4):253-264

BACKGROUND

Allergen immunotherapy (AIT) may have a long-term disease-modifying effect. The aim of this study was to demonstrate the long-term effects of pollen allergoid tyrosine-adsorbed subcutaneous AIT on allergic rhinitis (AR) and asthma (AA) in clinical practice.

METHODS

This retrospective study, funded by an AIT manufacturer, analysed the impact of AIT on AR progression and onset of need for AA medication, using a German database covering ~35% of national prescriptions during 2008-2020. Anonymized prescription data of AR patients aged 5-65 years treated with grass or tree pollen AIT between 2009 and 2013 and followed for at least 2 years after AIT cessation were compared with matched control patients with seasonal AR.

RESULTS

181,496 patients received AIT prescriptions. 5959 fulfilled the inclusion criteria. The median AIT treatment duration was 1092 days and the follow-up duration was 6.4 years. Less patients treated with AIT received prescriptions for symptomatic AR medication in the follow-up versus controls (AIT: OR: 0.37; 95% Confidence Interval (CI) 0.34, 0.40; p < .001, tyrosine adsorbed AIT: OR: 0.27; 95% CI 0.20, 0.35 p < .001). Less asthmatic patients under AIT received prescriptions for AA medications versus controls (AIT: OR: 0.48; 95% CI 0.41, 0.55; p < .001, tyrosine-adsorbed AIT: OR: 0.48; 95% CI 0.29, 0.79; p = .004). AR and AA medication prescriptions for AIT patients were reduced in the follow-up versus baseline and controls (AIT: AR: 20.0%; 1.5 vs. 0.2 prescriptions; AA: 29.1%; 2.0 vs. 0.6 prescriptions, p < .001; tyrosine-adsorbed AIT: AR: 24.2%, 1.4 vs. 0.2 prescriptions; AA: 35.6%, 2.1 vs. 0.6 prescriptions, p < .001). The probability of AA medication onset in non-asthmatic patients during follow up was reduced for AIT patients compared to controls (OR: 0.77, 95% CI 0.66, 0.90; p = .001). All endpoints were significant for children/adolescents and adults in stratified analyses.

CONCLUSIONS

We found evidence for long-term effects up to 9.5 years for tyrosine-adsorbed AIT.

4

Biomarcadores en mucosa nasal y respuesta a SLIT

Increased Nasal Blimp1 + Treg Cells After Sublingual Immunotherapy Reflect the Efficacy of Treatment in Allergic Rhinitis

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Adv Ther. 2024 Apr;41(4):1698-1710. doi: 10.1007/s12325-024-02819-8

INTRODUCTION

Allergen-specific immunotherapy (AIT) plays a pivotal role in altering the immune status and tissue responses in allergic rhinitis (AR). This study focuses on the impact of sublingual immunotherapy (SLIT) involving dust mite drops, exploring the modulation of regulatory T cells (Treg) and their specific marker, BLIMP1, in the nasal mucosa.

METHODS

Immune cells were isolated from nasal lavage fluid of patients with AR undergoing SLIT (n = 94). Treg cells were analyzed for BLIMP1 expression, and chemokine levels associated with Treg recruitment were assessed using Luminex assay. Patients were categorized on the basis of SLIT efficacy and followed for changes after discontinuation.

RESULTS

SLIT induced a significant increase in nasal Treg cells (7.09 ± 2.59% vs. 0.75 ± 0.27%, P < 0.0001). BLIMP1 expression in Treg cells notably increased after SLIT (0.36 ± 0.22% to 16.86 ± 5.74%, P < 0.0001). Ineffective SLIT cases exhibited lower levels of nasal Treg and Blimp1 + Treg cells (both P < 0.0001). Receiver operating characteristic (ROC) analysis confirmed their potential as efficacy predictors (AUC = 0.908 and 0.968, respectively). SLIT discontinuation led to a significant reduction in Treg and Blimp1 + Treg cells (P < 0.001), emphasizing their maintenance during treatment. Pro-inflammatory cytokines decreased (P < 0.001), while CCL2 associated with Treg recruitment increased (P = 0.0015).

CONCLUSION

Elevated nasal Blimp1 + Treg cells serve as a predictive biomarker for SLIT responsiveness in pediatric AR.Their influence on immunotherapy effectiveness contributes to a nuanced understanding of SLIT mechanisms, allowing for disease stratification and personalized treatment plans. This study offers scientific support for predicting SLIT efficacy, enhancing the prospects of improved treatment outcomes in AR.

5

La polisensibilización se asocia a síntomas más graves

Polysensitisation is associated with more severe symptoms: The reality of patients with allergy

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Clin Exp Allergy. 2024 Apr 27.doi: 10.1111/cea.14486

BACKGROUND

Studying the sensitisation profiles of patients with allergies allows for a deeper understanding of the disease which may facilitate the selection of the best-personalised allergen immunotherapy. This observational, cross-sectional, multicentre study aimed to demonstrate the heterogeneity of the German population with allergies by analysing specific immunoglobulin E (sIgE) patterns towards aeroallergens and exploring the relationship between sensitisation and clinical symptoms.

METHODS

In total, 500 patients with allergies from different regions of Germany were recruited based on their case histories, clinical allergic symptoms and skin prick test data for aeroallergens. Serum samples were analysed using ImmunoCAP assays to determine sIgE levels for 33 allergenic sources and 43 molecular allergens.

RESULTS

Most patients (81%) were polysensitised. Betula verrucosa pollen was the most common cause of sensitisation (59%), followed by Phleum pratense (58%) and Dermatophagoides pteronyssinus (44%). The highest prevalence rates of molecular allergens were observed for Bet v 1 (84%) from birch pollen, Phl p 1 from grass pollen (82%), Der p 2 (69%) from mites and Fel d 1 (69%) from cat. Polysensitisation was signifiantly associated with the presence of asthma and the severity of rhinitis symptoms.

CONCLUSIONS

Our findings show a high rate of polysensitisation and emphasise the importance of molecular diagnosis for more precise and comprehensive insights into sensitisation patterns and their association with clinical symptoms. These data may help improve personalised diagnosis and immunotherapy adapted to the needs of individual patients in the region.

6

ITA “hipoalergénica” frente a ácaros construida por IA

Construction by artificial intelligence and immunovalidation of hypoallergenic mite allergen Der f 36 vaccine

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Front Immunol. 2024 Mar 27:15:1325998. doi: 10.3389/fimmu.2024.1325998

BACKGROUND

The house dust mite (HDM) is widely recognized as the most prevalent allergen in allergic diseases. Allergen-specific immunotherapy (AIT) has been successfully implemented in clinical treatment for HDM. Hypoallergenic B-cell epitope-based vaccine designed by artificial intelligence (AI) represents a significant progression of recombinant hypoallergenic allergen derivatives.

METHOD

The three-dimensional protein structure of Der f 36 was constructed using Alphafold2. AI-based tools were employed to predict B-cell epitopes, which were subsequently verified through IgE-reaction testing. Hypoallergenic Der f 36 was then synthesized, expressed, and purified. The reduced allergenicity was assessed by enzyme-linked immunosorbent assay (ELISA), immunoblotting, and basophil activation test. T-cell response to hypoallergenic Der f 36 and Der f 36 was evaluated based on cytokine expression in the peripheral blood mononuclear cells (PBMCs) of patients. The immunogenicity was evaluated and compared through rabbit immunization with hypoallergenic Der f 36 and Der f 36, respectively. The inhibitory effect of the blocking IgG antibody on the specific IgE-binding activity and basophil activation of Der f 36 allergen was also examined.

RESULTS

The final selected non-allergic B-cell epitopes were 25-48, 57-67, 107-112, 142-151, and 176-184. Hypoallergenic Der f 36 showed significant reduction in IgE-binding activity. The competitive inhibition of IgE binding to Der f 36 was investigated using the hypoallergenic Der f 36, and only 20% inhibition could be achieved, which is greatly reduced when compared with inhibition by Der f 36 (98%). The hypoallergenic Der f 36 exhibited a low basophil-stimulating ratio similar to that of the negative control, and it could induce an increasing level of IFN-γ but not Th2 cytokines IL-5 and IL-13 in PBMCs. The vaccine-specific rabbit blocking IgG antibodies could inhibit the patients' IgE binding and basophil stimulation activity of Derf 36.

CONCLUSION

This study represents the first application of an AI strategy to facilitate the development of a B-cell epitope-based hypoallergenic Der f 36 vaccine, which may become a promising immunotherapy for HDM allergic patients due to its reduced allergenicity and its high immunogenicity in inducing blocking of IgG.

7

¡25 meta-análisis de ITA a examen!

A Meta-Analysis Investigating the Efficacy and Safety of Allergen-Specific Immunotherapy in the Management of Respiratory Allergies

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J Asthma. 2024 Apr 30:1-11. doi: 10.1080/02770903.2024.2349604

BACKGROUND

This meta-analysis aimed to evaluate the effectiveness and adverse effects of specific immunotherapy (SIT) in the management of respiratory allergens, including allergic asthma, rhinitis, and related disorders, based on a review of current literature up to November 8, 2022.

METHODS

We conducted a search of databases, including PubMed, Embase, Cochrane, and Web of Science, to identify relevant randomized controlled trials (RCTs) assessing respiratory allergy-specific immunotherapy. We employed the Consolidated Standards of Reporting Trials (CONSORT) Statement to select RCTs that adhered to rigorous reporting standards. Specifically, we focused on double blind placebo-controlled (DBPC) trials and open studies involving both adults and children, considering factors such as dosage, inclusion criteria, allergens, and primary outcome measurements.

RESULTS

A total of 25 meta-analyses were included in this study. Among them, 14 evaluated sublingual specific allergen immunotherapy (SLIT), 4 assessed subcutaneous allergen immunotherapy (SCIT), 4 explored both sublingual and subcutaneous immunotherapy, and 3 investigated intralymphatic immunotherapy. The outcomes of these meta-analyses indicated a reduction in medication scores in 20 cases and a decrease in symptom scores in 23 cases. Additionally, six studies reported on changes in IgE levels, seven studies focused on IgG4, four studies examined FEV1 (forced expiratory volume in one second), and eight studies reported on symptom and medication scores. Furthermore, eleven studies reported on differences in adverse reactions.

CONCLUSION

The results of our meta-analysis suggest that specific immunotherapy, while associated with some adverse effects, effectively reduces the symptoms of asthma and rhinitis. Therefore, we recommend its use in the treatment of respiratory allergies.

8

Cómo validar una cámara de exposición ambiental controlada

Clinical validation of grass pollen exposure chamber in patients with allergic rhinitis triggered by timothy grass

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Clin Exp Allergy. 2024 Apr 14. doi: 10.1111/cea.14482

BACKGROUND

The fluctuation in concentrations of airborne allergens frequently presents a challenge to assessing the efficacy of allergen immunotherapy (AIT) in 'field' studies. Allergen exposure chambers (AECs) are specialized medical installations developed to expose individuals to allergens at defined and consistent concentrations under a controlled environment. The aim of the study was to validate the provocation test with timothy grass pollen as well as to assess its safety in the AEC in patients with allergic rhinitis.

METHODS

In the ALLEC® AEC, varying concentrations of timothy grass pollen were dispersed. Allergic symptoms were measured by total nasal symptom score (TNSS), acoustic rhinometry, peak nasal inspiratory flow (PNIF) and nasal discharge volume. Lung function, assessed through peak expiratory flow rate (PEFR) and forced expiratory volume in the first second (FEV1), was used to evaluate safety.

RESULTS

The consistency of the test was proved by the stability of environmental conditions, including temperature, humidity and CO2 levels, as well as constant concentrations of grass pollen at predetermined levels ranging from 1000 to 10,000 particles per cubic meter (p/m3). Allergic individuals developed symptoms at concentrations of 3000 p/m3 and above, across all measured endpoints. Lung function was not affected throughout all the challenges. The reproducibility of symptoms was confirmed throughout the tests. The concentration of 8000 p/m3 together with a challenge duration of 120 min was found to be optimal.

CONCLUSION

The study demonstrates that the ALLEC® grass pollen exposure chamber provides a reliable and safe method for inducing repeatable symptoms in patients with allergic rhinitis. This approach can be effectively applied for allergy diagnostics and clinical endpoint determination during AIT.

9

Buscando consenso para la reactividad cruzada provocada por la tropomiosina

Toward Consensus Epitopes B and T of Tropomyosin Involved in Cross-Reactivity across Diverse Allergens: An In Silico Study

Dalgys Martínez, Luis Fang, Catherine Meza-Torres, Gloria Garavito, Guillermo López-Lluch, Eduardo Egea

Biomedicines. 2024 Apr 17;12(4):884.doi: 10.3390/biomedicines12040884

ABSTRACT

Tropomyosin (TM) is a pan-allergen with cross-reactivity to arthropods, insects, and nematodes in tropical regions. While IgE epitopes of TM contribute to sensitization, T-cell (MHC-II) epitopes polarize the Th2 immune response. This study aimed to identify linear B and T consensus epitopes among house dust mites, cockroaches, Ascaris lumbricoides, shrimp, and mosquitoes, exploring the molecular basis of cross reactivity in allergic diseases. Amino acid sequences of Der p 10, Der f 10, Blo t 10, Lit v 1, Pen a 1, Pen m 1, rAsc l 3, Per a 7, Bla g 7, and Aed a 10 were collected from Allergen Nomenclature and UniProt. B epitopes were predicted using AlgPred 2.0 and BepiPred 3.0. T epitopes were predicted with NetMHCIIpan 4.1 against 10 HLA-II alleles. Consensus epitopes were obtained through analysis and Epitope Cluster Analysis in the Immune Epitope Database. We found 7 B-cell epitopes and 28 linear T-cell epitopes binding to MHC II. A unique peptide (residues 160-174) exhibited overlap between linear B-cell and T-cell epitopes, highly conserved across tropomyosin sequences. These findings shed light on IgE cross-reactivity among the tested species. The described immuno-informatics pipeline and epitopes can inform in vitro research and guide synthetic multi-epitope proteins' design for potential allergology immunotherapies. Further in silico studies are warranted to confirm epitope accuracy and guide future experimental protocols.

10

Edadismo y alergia a himenópteros

Elderly Patients and Insect Venom Allergy: Are the Clinical Pictures and Immunological Parameters of Venom Allergy AgeDependent?

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Vaccines (Basel). 2024 Apr 9;12(4):394. doi: 10.3390/vaccines12040394

ABSTRACT

Insect venom is one of the most common triggers of anaphylaxis in the elderly population. Venom immunotherapy (VIT) remains the only treatment for Hymenoptera venom allergy (HVA). However, little is known about the differences in indication for VIT in the group of patients aged 60 years and older. The objective of this study was to assess the clinical and diagnostic differences of HVA in elderly patients. The study compared data from patients aged ≥ 60 (N = 132) to data from patients aged from 11 to 60 years (N = 750) in terms of HVA severity, comorbidities, and immunological parameters, namely, intradermal testing (IDT), specific IgE (sIgE) levels against extracts and major allergenic molecules, and serum tryptase level (sBT). The severity of systemic HVA (I-IV Müller scale) did not differ between adults and seniors. However, the severity of cardiovascular reactions (IV) increased with age, while the frequency of respiratory reactions (III) decreased. No differences were found in the immunological parameters of sensitization IDT, venom specific IgE concentrations, or sIgE against Api m 1, 2, 4, 5, and 10 between patients below and above 60 or 65 years of age. Differences were noted for sIgE against Ves v1 and Ves v5; they were higher and lower, respectively, in seniors. In the seniors group, sBT levels were higher. Elevated tryptase levels, along with the aging process, can represent a risk factor within this age category. Nevertheless, advanced age does not influence the immunological parameters of immediate HVA reactions, nor does it impact the diagnosis of HVA. Hymenoptera venom allergy (HVA); elderly people; immunological parameters; immunotherapy.

1

Recomendaciones para dar en la diana con la IT intralinfática

How to hit the allergy target: A critical appraisal of intralymphatic immunotherapy with practical recommendations on ultrasoundguided injections

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Allergy. 2024 May 7. doi: 10.1111/all.16138. Epub ahead of print. PMID: 38712754

BACKGROUND

Intralymphatic immunotherapy (ILIT) represents a promising novel approach treating allergic diseases. However, no standardized procedures or recommendations have been established or reported, despite the recognized fact that treatment efficacy relies on the ability to inject the allergen intranodally.

OBJECTIVE

We aim to provide a critical appraisal of ILIT as a method of allergen immunotherapy and to deliver practical recommendations for accurate ILIT.

METHODS

One hundred and seventy-three ILIT injections were performed in 28 (47%) women and 32 (53%) men with median age of 29 years (21-59). The injections were ultrasound-guided and recorded for retrospective analysis with respect to injection location, needle visibility, medication release, and patient characteristics.

RESULTS

The results show that the correct positioning of the needle within the lymph node (LN) was most critical. If the whole length of the needle bevel was not inserted into the LN, substance backflush into the interstitium was observed. Selecting a more superficial LN and inserting the needle at a smaller angle towards the LN significantly improved needle visibility in the ultrasound. Longitudinal results showed that continuous practice significantly correlated with improved needle visibility and more accurate ILIT injections.

CONCLUSION

Based on our results and practical experience, we propose several recommendations for LN selection and the correct handling of ultrasound probe and needle. We are confident that ILIT standardization and training will be important as to meet the goals of good safety and efficacy of ILIT.

2

Centremos la APPtención en el paciente

Digitally-enabled, person-centred care (PCC) in allergen immunotherapy: An ARIA-EAACI Position Paper

Pfaar O, Sousa-Pinto B, Papadopoulos NG, Larenas-Linnemann DE, Ordak M, Torres MJ, et al

Allergy. 2024 May 3. doi: 10.1111/all.16135. Epub ahead of print. PMID: 38700063

ABSTRACT

In rhinitis and asthma, several mHealth apps have been developed but only a few have been validated. However, these apps have a high potential for improving person-centred care (PCC), especially in allergen immunotherapy (AIT). They can provide support in AIT initiation by selecting the appropriate patient and allergen shared decision-making. They can also help in (i) the evaluation of (early) efficacy, (ii) early and late stopping rules and (iii) the evaluation of (carried-over) efficacy after cessation of the treatment course. Future perspectives have been formulated in the first report of a joint task force (TF)-Allergic Rhinitis and Its Impact on Asthma (ARIA) and the European Academy of Allergy and Clinical Immunology (EAACI)-on digital biomarkers. The TF on AIT now aims to (i) outline the potential of the clinical applications of mHealth solutions, (ii) express their current limitations, (iii) make proposals regarding further developments for both clinical practice and scientific purpose and (iv) suggest which of the tools might best comply with the purpose of digitally-enabled PCC in AIT.

3

Efectividad a largo plazo de SLIT con ácaros, clínica y ... en función pulmonar!!

Long-term efficacy of house dust mite sublingual immunotherapy on clinical and pulmonary function in patients with asthma and allergic rhinitis

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J Allergy Clin Immunol Glob. 2024 Jan 6;3(2):100206. doi: 10.1016/j.jacig.2024.100206. PMID: 38328802; PMCID: PMC10847160

BACKGROUND

A previous study reported that house dust mite (HDM) sublingual immunotherapy (SLIT) for 48 weeks was effective as add-on treatment for allergic asthma; however, data regarding its long-term efficacy are scarce.

OBJECTIVE

We sought to evaluate the effect of HDM SLIT on asthma control, pulmonary function, and airway inflammation and remodeling throughout the 5-year treatment period.

METHODS

A total of 140 patients with asthma and allergic rhinitis sensitized to HDM were randomized to receive either drugs alone or drugs plus SLIT for 5 years. The 5-item Asthma Control Questionnaire (ACQ-5), Asthma Quality of Life Questionnaire (AQLQ), Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), spirometry, quantitative computed tomography, and type 2 biomarkers were assessed.

RESULTS

An improvement in the ACQ-5, AQLQ, and RQLQ scores was observed in the SLIT group compared with the control group. HDM SLIT increased lung function and reduced the percentage of airway wall area. The levels of fractional exhaled nitric oxide (Feno), blood eosinophil, serum specific IgE for HDM, and total IgE decreased and were sustained during the 5 years. The change in type 2 biomarkers correlated with change in the AQLQ score. On the basis of receiver-operating characteristic analysis for predicting responders, the area under the receiver-operating characteristic curve in FEV1% predicted, airway wall area, Feno, and specific IgE was high. Multivariate regression analysis showed that the strongest predictor of responders was Feno.

CONCLUSIONS

HDM SLIT continued to provide sustained efficacy, improve lung function, and prevent progression of airway inflammation and remodeling in asthma throughout the 5-year treatment period.

4

La SLIT en presentación “líquida”, a la palestra

IR (index of reactivity)-house dust mite sublingual immunotherapy liquid formulation for allergic rhinoconjunctivitis: Systematic review and meta-analysis of randomized and nonrandomized studies

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J Allergy Clin Immunol Glob. 2024 Jan 9;3(2):100208. doi: 10.1016/j.jacig.2024.100208. PMID: 38328804; PMCID: PMC10847924

BACKGROUND

Although randomized controlled trials (RCT) are the reference standard of evidence in allergen immunotherapy (AIT), nonrandomized studies (NRS) are needed to confirm their results in more representative populations, particularly for treatment duration and persistence. However, when discrepancies are observed between RCT and NRS, NRS reliability decreases because these discrepant results are generally attributed to the methodologic flaws of NRS.

OBJECTIVE

We compared the benefit of sublingual AIT (SLIT) for allergic rhinoconjunctivitis in NRS versus RCT focusing on a single product/allergen to reduce heterogeneity.

METHODS

For meta-analysis, house dust mite (HDM) SLIT liquid formulation studies were sourced from computerized (Medline, Web of Science, and LILACS databases, to January 2023) and manual literature searches. Populations, treatments, and outcome data were combined (DerSimonian-Laird method). Noncomparative NRS were compared to RCT' SLIT arm before and after treatment. Efficacy was determined as the standardized mean difference (SMD) in symptom score (SS) and medication score (MS).

RESULTS

Data from 12 NRS (682 patients) and 8 RCT (176 patients) were analyzed. The benefit with index of reactivity (IR)-HDM SLIT liquid formulation was found significant for, first, SS in both NRS (SMD = -1.27; 95% confidence interval [CI], -1.64, -0.90) and RCT (SMD = -0.56; 95% CI, - 0.90, -0.21), and second, MS with SMD equal to -1.35 (95% CI, -1.77, -0.93) and -0.46 (95% CI, -0.67, -0.25), respectively. Metaregression showed that symptom improvement was correlated with treatment duration with consistent results in NRS and RCT with 12 month SS data: -0.87 (interquartile range, -1.02, -0.77) and -0.75 (interquartile range, -0.93, -0.41), respectively.

CONCLUSION

This meta-analysis showed comparable clinical benefit of IR-HDM SLIT liquid formulation increasing over time in both NRS and RCT, suggesting that NRS may reliably integrate RCT results and be considered for guidelines.

5

ITO a cacahuete con liofilizado horneado. ¿Alternativa “hipoalergénica”?

Peanut oral immunotherapy using an extensively heated and baked novel composition of peanuts

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Pediatr Allergy Immunol. 2024 May;35(5):e14146. doi: 10.1111/pai.14146. PMID: 38783409

BACKGROUND

Oral immunotherapy (OIT) is an increasingly acceptable therapeutic option for peanut-allergic (PA) children, despite significant side effects. Major peanut allergenic proteins are heat-resistant and are not rendered hypoallergenic after baking or cooking. Lyophilized peanut proteinMH (LPP-MH) is a novel composition from developing peanuts, enabling cooking-induced reduction in allergenicity. We aimed to explore the safety and efficacy of OIT, with extensively heated and baked (EHEB) LPP-MH in PA children.

METHODS

In a single-arm, single-center, pilot study, PA children with a single highest tolerated dose of <100 mg peanut protein were placed on a 40-week OIT protocol with 300 mg daily of heat-treated LPP-MH. A repeat open peanut food challenge was performed after 40 weeks of treatment and at a 6-12 months of follow-up visit.

RESULTS

Thirty-three children with PA were enrolled, with a mean cumulative tolerated dose (MCTD) of 71.2 mg PP (95% CI 45-100 mg). After 40 weeks, 32/33 patients were able to consume more than 300 mg of natural PP, with MCTD of 1709 mg (CI 365 3675 mg). There were no severe allergic reactions requiring epinephrine, during any of the observed LPP-MH challenges or any treatment related doses at home. After 6-12 months on daily maintenance, the MCTD was 8821 mg (95% CI 1930 13,500 mg). This enabled most children age-appropriate dietary inclusion of peanuts.

CONCLUSION

An OIT protocol with heat-treated LPP-MH, a novel composition from developing peanuts, seems a potentially safe and efficacious OIT modality for PA children, enabling the introduction of dietary levels of peanut proteins in highly allergic PA children. Validation in randomized controlled studies is mandated.

6

Repasando la efectividad de ITO + biológico en la alergia a alimentos

Immunotherapy and biologics in the management of IgE-mediated food allergy: Systematic review and meta-analyses of efficacy and safety

Riggioni C, Oton T, Carmona L, Du Toit G, Skypala I, Santos AF

Allergy. 2024 May 15. doi: 10.1111/all.16129. Epub ahead of print. PMID: 38747333

ABSTRACT

Food allergy (FA) is a potentially life-threatening chronic condition that is becoming an increasing public health problem worldwide. This systematic review (SR) was carried out to inform the development of clinical recommendations on the treatment of IgE mediated FA with biologics and/or IT for the update of the EAACI guidelines. A SR of randomized controlled trials or quasi-controlled trials was carried out. Studies were identified via comprehensive search strategies in Medline, Embase, and Cochrane Library, up to April 2022.

POPULATION

Population: Human adults, children, and adolescents with IgE-mediated FA. Intervention: IT and/or biologics.

COMPARATOR

Placebo or standard-of-care (allergen avoidance).

OUTCOMES

Efficacy (desensitization, sustained unresponsiveness (SU), remission), quality of life, and safety (systemic and local adverse reactions (AR)). The Cochrane RoB tool was used to assess the risk of bias. It was reported according to PRISMA and registered in PROSPERO CRD4202229828. After screening, 121 studies were included (111 for IT and 10 for biologics). Most studies had a high risk of bias and showed high heterogeneity in design and results. Metanalysis showed a positive effect of biologics and IT in terms of relative risk (RR) for achieving tolerance to the culprit food compared to avoidance or placebo. Omalizumab for any FA showed a RR of 2.17 [95% confidence interval: 1.22, 3.85]. For peanut allergy, oral IT (OIT) had a RRof 11.94 [1.76, 80.84] versus avoidance or placebo, sublingual IT (SLIT) had a RR of 3.00 [1.04, 8.66], and epicutaneous IT (EPIT) of 2.16 [1.56, 3.00]. OIT had a RR of 5.88 [2.27, 15.18] for cow's milk allergy, and of 3.43 [2.24, 5.27] for egg allergy. There was insufficient data on SLIT or EPIT for the treatment of egg and milk allergies. Most ARs reported were mild. For OIT the most common AR involved the gastrointestinal system and for EPIT, AR's most commonly affected the skin. There was limited data on severe or life-threatening ARs. There was limited evidence for long term efficacy and quality of life. In conclusion, biologics and IT, alone or in combination, are effective in achieving desensitization while on active treatment but more evidence is needed on long-term tolerance as current evidence is not of high quality. Adverse events while on therapy are generally mild to moderate but a long-term comprehensive safety profile is missing. There is a critical need to optimize and standardize desensitization protocols and outcome measures to facilitate our understanding of the efficacy and safety as well as to allow for comparison between interventions.

7

¿Y si usamos los comprimidos de IT también para medir respuesta en provocaciones nasales?

Utility of silver birch and house dust mite extracts derived from licensed sublingual tablets for nasal allergen challenge

Olivieri B, Gil AJ, Stoenchev K, Durham SR, Scadding G

Clin Transl Allergy. 2024 May;14(5):e12360. doi: 10.1002/clt2.12360. PMID: 38779783; PMCID: PMC11112400

BACKGROUND

Nasal allergen challenge (NAC) is used to investigate the effects of allergen exposure and assess treatment efficacy in allergic rhinitis (AR). This study aims to establish dose-responses to NAC using licensed silver birch (SB) pollen and house dust mite (HDM) sublingual tablets as sources of the allergen extracts in participants with AR.

METHODS

Sixteen volunteers with HDM-induced perennial AR and 15 volunteers with SB pollen-induced seasonal rhinitis underwent a graded updosing NAC with extracts derived from HDM allergen (Acarizax®) and SB (Itulazax®) tablets, respectively. Total nasal symptom score (TNSS, range 0- 12) and peak nasal inspiratory flow (PNIF) were recorded before, at 10 min and at the end of the NAC. The dose of each allergen that provoked a TNSS of at least 7 ("provoking dose 7") in most allergic participants was identified. NACs using the "provoking dose 7" were performed on 5 nonallergic individuals to test for irritant effects. The "provoking dose 7" of HDM extract was used in a subgroup of two SB allergic, non HDM allergic, volunteers, and vice versa for SB extract, to test for allergen specificity of the responses.

RESULTS

Most patients experienced a TNSS of at least 7/12 at a median concentration of 1500 AU/mL for both SB pollen and HDM. The average decline in PNIF at this dose was 63.15% for SB and 63.99% for HDM. NACs using the 1500 AU/mL concentrations were performed on 5 non-allergic individuals with no symptomatic or PNIF response. 1500 AU/mL of HDM extract produced no symptoms in SB allergics nor 1500 AU/mL SB extract in HDM allergics.

CONCLUSION

For both SB and HDM extracts, the optimal allergen dose for NAC to cause a moderate-severity response ("provoking dose 7/12") was 1500 AU/mL. Licensed sublingual allergen tablets provide a readily available and inexpensive source of SB and HDM extracts for use in future interventional studies in AR.

8

Las pautas ultra-rápidas con avispa también funcionan a partir de los 60

Safety and Efficacy of VIT against Wasp Venom in Ultra-Rush Protocols in Patients Older Than 60 Years

Bożek A, Winterstein J, Pawłowicz R, Poians I, Sadowska D, Miodonska M, Nittner-Marszalska M

Vaccines (Basel). 2024 May 16;12(5):547. doi: 10.3390/vaccines12050547. PMID: 38793798; PMCID: PMC11125965

BACKGROUND

Allergen immunotherapy remains a widely recognized and widely used method for the treatment of selected allergic diseases. Currently, according to the European Academy Of Allergy and Clinical Immunology (EAACI) guidelines, venom immunotherapy (VIT) may be considered for patients over 60. Nevertheless, no separate studies have confirmed the efficacy and safety of this therapy. This study aimed to evaluate the short-term effectiveness of VIT against wasp allergens in an ultra-rush protocol for older patients compared to young patients.

METHODS

Among the 113 patients included in this study, 51 were older than 60 years (Group A), and 62 formed the control "young group" (age range: 18-35 years). All patients were desensitized to wasp venom using the ultra-rush protocol according to Muller and aqueous solutions of vaccines containing wasp venom. A basophil activation test (Basotest, Orpegen Pharma, Germany) and intracutaneous tests with dilutions of wasp allergen and specific IgE to extract wasp venom were performed at the start and after six months of VIT. The safety of VIT was assessed on the basis of the international Mueller scale.

RESULTS

One hundred and eleven patients with confirmed wasp allergies completed six months of VIT: 51 participants over 60 years of age (Group A) and 60 young people (Group B). No systemic adverse reactions were observed during the VIT induction phase. However, large local reactions were noted in 17% of older patients and 20% of young patients at a similar level ($p > 0.05$). During maintenance VIT, two mild grade I systemic reactions were confirmed in young patients. These symptoms resolved spontaneously. There were no such reactions in older patients. The effectiveness of VIT was tested using BAT. There was a statistically significant reduction in CD63 reactivity in 86% of patients in Group A, and a comparable and substantial decrease in 84% of young patients in Group B. According to the BAT test, the mean reductions in the area under the curve (AUC) after six months of VIT were significant ($p < 0.05$) and comparable between Groups A and B: -6.52 vs. 7.21.

CONCLUSIONS

VIT against wasp venom is safe and effective in short-term observation, and is comparable to that used for young patients.

9

ITO en cápsulas para la alergia a ácaros, ¿incluso mejor que SCIT?

Oral immunotherapy with enteric-coated capsules for allergic rhinitis caused by house dust mites

Zhang HZ, Xie W, Zhou WC , Chen J, Wang Y, Zhu YY, Wen TH, Cheng L
Front Allergy. 2024 May 7;5:1345929. doi: 10.3389/falgy.2024.1345929. PMID: 38774588; PMCID: PMC11106396

BACKGROUND
Oral immunotherapy (OIT) is a promising allergen-specific approach in the management of food allergy; however, studies on OIT for allergic rhinitis (AR) have rarely been reported. The purpose of this study is to evaluate the efficacy and safety of OIT using enteric-coated capsules for AR induced by house dust mites.

METHODS
A total of 49 patients with AR were enrolled, including 25 who received subcutaneous immunotherapy (SCIT) and 24 who received OIT. The clinical efficacy and safety in both groups were evaluated.

RESULTS
After 1 year of treatment, both SCIT and OIT demonstrated significant therapeutic effects. OIT was found to be more effective than SCIT in reducing the total AR symptom score and improving the results of nasal provocation tests. Local and systemic adverse reactions were observed in the SCIT group, while none were reported in the OIT group.

CONCLUSION
OIT is an effective and safe treatment for mite induced AR.

10

La cucaracha (y su ITA) necesita ayuda para “caminar”

A pediatric randomized, controlled trial of German cockroach subcutaneous immunotherapy

Zoratti E, Wood R, Pomés A, Da Silva Antunes R, Altman MC et al
J Allergy Clin Immunol. 2024 May 6:S0091-6749(24)00455-X. doi: 10.1016/j.jaci.2024.04.022. Epub ahead of print. PMID: 38718950

BACKGROUND
Cockroach allergy contributes to morbidity among urban children with asthma. Few trials address the effect of subcutaneous immunotherapy (SCIT) with cockroach allergen among these at-risk children.

OBJECTIVE
To determine if nasal allergen challenge (NAC) responses to cockroach allergen would improve following one year of SCIT.

METHODS
Urban children with asthma, that were cockroach-sensitized and reactive on NAC, participated in a yearlong randomized double-blind placebo-controlled SCIT trial using German cockroach extract. The primary endpoint was the change in mean total nasal symptoms scores (TNSS) during NAC after 12 months of SCIT. Changes in nasal transcriptomic responses during NAC, skin prick test (SPT) wheal size, serum allergen-specific antibody production and T-cell responses to cockroach allergen were assessed.

RESULTS
Changes in mean NAC TNSS did not differ between SCIT-assigned (n=28) versus placebo-assigned (n=29) participants (p=0.63). Nasal transcriptomic responses correlated with TNSS, but a treatment effect was not observed. Cockroach serum specific IgE (sIgE) decreased to a similar extent in both groups, while decreased cockroach SPT wheal size was greater among SCIT participants (p=0.04). A 200-fold increase in cockroach sIgG4 was observed among subjects receiving SCIT (p<0.001) but was unchanged in the placebo group. T-cell interleukin-4 responses following cockroach allergen stimulation decreased to a greater extent among SCIT versus placebo (p=0.002), while no effect was observed for interleukin-10 or interferon-gamma.

CONCLUSION
A year of SCIT failed to alter NAC TNSS and nasal transcriptome responses to cockroach allergen challenge despite systemic effects on allergen-specific skin tests, induction of serum sIgG4 production and down-modulation of allergen stimulated T cell responses.

1

Delphi internacional sobre ITO para establecer unas bases comunes

Preparing patients for oral immunotherapy (PPOINT): international delphi consensus for procedural preparation and consent

Douglas P Mack, Timothy E Dribin, Paul J Turner, Richard L Wasserman, Mariam A Hanna, Marcus Shaker et al

J Allergy Clin Immunol. 2024 Jun;153(6):1621-1633

BACKGROUND

Despite the promise of oral immunotherapy (OIT) to treat food allergies, this procedure is associated with potential risk. There is no current agreement about what elements should be included in the preparatory or consent process.

OBJECTIVE

We developed consensus recommendations about the OIT process considerations and patient-specific factors that should be addressed before initiating OIT and developed a consensus OIT consent process and information form.

METHODS

We convened a 36-member Preparing Patients for Oral Immunotherapy (PPOINT) panel of allergy experts to develop a consensus OIT patient preparation, informed consent process, and framework form. Consensus for themes and statements was reached using Delphi methodology, and the consent information form was developed.

RESULTS

The expert panel reached consensus for 4 themes and 103 statements specific to OIT preparatory procedures, of which 76 statements reached consensus for inclusion specific to the following themes: general considerations for counseling patients about OIT; patient- and family-specific factors that should be addressed before initiating OIT and during OIT; indications for initiating OIT; and potential contraindications and precautions for OIT. The panel reached consensus on 9 OIT consent form themes: benefits, risks, outcomes, alternatives, risk mitigation, difficulties/challenges, discontinuation, office policies, and long-term management. From these themes, 219 statements were proposed, of which 189 reached consensus, and 71 were included on the consent information form.

CONCLUSION

We developed consensus recommendations to prepare and counsel patients for safe and effective OIT in clinical practice with evidence-based risk mitigation. Adoption of these recommendations may help standardize clinical care and improve patient outcomes and quality of life.

2

IgG4: biomarcardor confirmado de efectividad en ITO con cacahuete

Neutralizing IgG4 antibodies are a biomarker of sustained efficacy after peanut oral immunotherapy

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J Allergy Clin Immunol. 2024 Jun;153(6):1611-1620.e7

BACKGROUND

Clinical efficacy of oral immunotherapy (OIT) has been associated with the induction of blocking antibodies, particularly those capable of disrupting IgE-allergen interactions. Previously, we identified mAbs to Ara h 2 and structurally characterized their epitopes.

OBJECTIVE

We investigated longitudinal changes during OIT in antibody binding to conformational epitopes and correlated the results with isotype and clinical efficacy.

METHODS

We developed an indirect inhibitory ELISA using mAbs to block conformational epitopes on immobilized Ara h 2 from binding to serum immunoglobulins from peanut-allergic patients undergoing OIT. We tested the functional blocking ability of mAbs using passive cutaneous anaphylaxis in mice with humanized FcεRI receptors.

RESULTS

Diverse serum IgE recognition of Ara h 2 conformational epitopes are similar before and after OIT. Optimal inhibition of serum IgE occurs with the combination of 2 neutralizing mAbs (nAbs) recognizing epitopes 1.2 and 3, compared to 2 nonneutralizing mAbs (nonnAbs). After OIT, IgG4 nAbs, but not IgG1 or IgG2 nAbs, increased in sustained compared to transient outcomes. Induction of IgG4 nAbs occurs after OIT only in those with sustained efficacy. Murine passive cutaneous anaphylaxis after sensitization with pooled human sera is significantly inhibited by nAbs compared to non-nAbs.

CONCLUSIONS

Serum IgE conformational epitope diversity remains unchanged during OIT. However, IgG4 nAbs capable of uniquely disrupting IgE-allergen interactions to prevent effector cell activation are selectively induced in OIT-treated individuals with sustained clinical efficacy. Therefore, the induction of neutralizing IgG4 antibodies to Ara h 2 are clinically relevant biomarkers of durable efficacy in OIT.

3

La ITSL previene el asma y el empeoramiento de la rinitis

Impact of liquid sublingual immunotherapy on asthma onset and progression in patients with allergic rhinitis: a nationwide population-based study (EfficAPSI study)

Pascal Demoly, Mathieu Molimard, Jean-François Bergmann, Bertrand Delaisi, Amandine Gouverneur Jade Vadel et al

Lancet Reg Health Eur . 2024 Apr 26:41:100915

BACKGROUND

The only disease-modifying treatment currently available for allergic rhinitis (AR) is allergen immunotherapy (AIT). The main objective of the EfficAPSI real-world study (RWS) was to evaluate the impact of liquid sublingual immunotherapy (SLIT-liquid) on asthma onset and evolution in AR patients.

METHODS

An analysis with propensity score weighting was performed using the EfficAPSI cohort, comparing patients dispensed SLIT-liquid with patients dispensed AR symptomatic medication with no history of AIT (controls). Index date corresponded to the first dispensation of either treatment. The sensitive definition of asthma event considered the first asthma drug dispensation, hospitalisation or long-term disease (LTD) for asthma, the specific one omitted drug dispensation and the combined one considered omalizumab or three ICS ± LABA dispensation, hospitalisation or LTD. In patients with pre existing asthma, the GINA treatment step-up evolution was analysed.

FINDINGS

In this cohort including 112,492 SLIT-liquid and 333,082 controls, SLIT-liquid exposure was associated with a significant lower risk of asthma onset vs. control, according to all definitions (combined: HR [95% CI] = 0.62 [0.60-0.63], sensitive: 0.77 [0.76-0.78], and specific: 0.67 [0.61-0.72]). Exposure to SLIT was associated with a one-third reduction in GINA step-up regardless baseline steps.

INTERVENTIONS

In this national RWS with the largest number of person-years of follow-up to date in the field of AIT, SLIT liquid was associated with a significant reduction in the risk of asthma onset or worsening. The use of three definitions (sensitive or specific) and GINA step-up reinforced the rigorous methodology, substantiating SLIT-liquid evidence as a causal treatment option for patients with respiratory allergies.

4

La IT con tabletas mejora la calidad de vida en pacientes con rinoconjuntivitis

Sublingual tablet immunotherapy improves quality of life in adults with allergic rhinoconjunctivitis

Michael S Blaiss, Stephen R Durham, David Bernstein, Thomas Stranzl, Morten Lindholm, Hendrik Nolte et al

J Allergy Clin Immunol Pract . 2024 Jun;12(6):1520-1529.e5

BACKGROUND

Allergic rhinitis with or without conjunctivitis can negatively impact many aspects of quality of life (QoL). The efficacy and safety of standardized quality (SQ) sublingual immunotherapy (SLIT) tablets have been confirmed across large clinical trials in adults with grass, tree, ragweed, and house dust mite (HDM) allergic rhinitis with or without conjunctivitis.

OBJECTIVE

This pooled analysis investigates whether the reduction in symptom burden found across the clinical trials is supported by improvements in QoL.

METHODS

A total of 11 phase II/III randomized placebo controlled trials across the SQ grass, tree, ragweed, and HDM SLIT tablets (grass: N = 3179; ragweed: N = 767; tree: N = 634; HDM: N = 2221) were included. QoL was assessed using the standardized Rhinitis Quality of Life Questionnaire (RQLQ), with the exception of 3 grass trials, which used the nonstandardized version. The overall RQLQ scores were expressed as a mean of 7 domains. In the pooled analysis, treatment was used as fixed effect; and the trial, and the interaction between region/country and trial as random effects.

RESULTS

The pooled analysis showed consistent and statistically significant improvements in overall RQLQ scores across all 4 SQ SLIT tablets versus placebo (pooled estimate [95% CI], P value grass: -0.20 [-0.28 to -0.12], P < .001; tree: -0.42 [-0.58 to -0.26], P < .001; ragweed: -0.36 [-0.55 to -0.17], P < .001; HDM: -0.28 [-0.39 to -0.17], P < .001). Furthermore, significant improvements versus placebo for all 4 SQ SLIT tablets were seen across the 7 individual domains.

CONCLUSIONS

The proven efficacy of SQ SLIT tablets to reduce symptoms across 4 of the most common respiratory allergens is supported by concurrent significant improvements in RQLQ scores overall and for all 7 domains.

5

Revisando la efectividad de la ITO con leche y/o huevo horneado, se “desinfla” la euforia

The safety and efficacy of baked egg and milk dietary advancement therapy: a systematic review and metaanalysis

Aikaterini Anagnostou, Douglas P Mack, Stephanie Johannes, Marcus Shaker, Elissa M Abrams

J Allergy Clin Immunol Pract . 2024 Jun 18:S2213-2198(24)00639-1

BACKGROUND

Cow's milk and egg allergy affect approximately 1.9% and 0.9% of children, respectively. Dietary advancement therapies (DAT), including milk (ML) and egg (EL) ladders, baked milk (BM-OIT) and baked egg (BE-OIT) oral immunotherapy are potential therapeutic options for these patients.

OBJECTIVE

To perform systematic review and meta-analysis of the safety and efficacy of DAT in children with IgE mediated milk or egg allergy.

METHODS

A systematic literature review was conducted, exploring 22 potential outcomes, with meta-analysis performed where >3 studies reported data. The GRADE approach was used to determine the certainty of evidence for each outcome, and the Johanna Briggs Institute tools for determining risk of bias.

RESULTS

Twenty-nine studies met inclusion criteria among 9946 titles screened. Tolerance occurred in 69% of EL, 58% of ML, 49% of BEOIT and 29% of BM-OIT patients. All severity allergic reactions occurred in 21% of EL, 25% of ML, 20% of BE-OIT and 61% of BM-OIT patients, with epinephrine use in 3% of EL, 2% of ML, and 9% of BM-OIT patients. At-home reactions occurred in 19% of BE-OIT and 10% of BM-OIT patients. Discontinuation occurred in 14% of EL, 17% of ML, 17% of BE-OIT and 20% of BM-OIT patients. Mean time to BE egg and BE-OIT tolerance was 13.25 months (4 studies) and 19.1 months (3 studies). Certainty of evidence was very low, and risk of bias high. Study heterogeneity was high, attributable to multiple factors.

CONCLUSIONS

There is very low certainty of evidence supporting DAT safety and efficacy. We cannot conclude DAT accelerates tolerance development.

6

Busquemos tratamientos comunes (para DA y alergia a alimentos) que además prevengan la marcha atópica

Atopic dermatitis and IgE-mediated food allergy: common biologic targets for therapy and prevention

H Mark Kenney, Jennifer Battaglia, Katherine Herman, Lisa A Beck

Atopic dermatitis; atopic march; biologics; clinical trials; epithelial barrier; food allergy; pediatrics; prevention; remission; sensitization; sustained unresponsiveness; type 2 immunity

OBJECTIVE

To highlight common mechanistic targets for the treatment of atopic dermatitis (AD) and IgE-mediated food allergy (IgE-FA) with potential to be effective for both diseases and prevent atopic progression.

DATA SOURCE

PubMed searches or NCT-registered clinical trials related to AD, IgE-FA, and other atopic conditions, especially focused on the pediatric population.

STUDY SELECTION

Human seminal studies and/or articles published in the past decade were emphasized with reference to pre-clinical models when relevant. NCT-registered clinical trials were filtered by inclusion of pediatric subjects <18-years of age with special focus on children <12-years as a critical period when AD and IgE-FA diseases may often be concurrent.

RESULTS

AD and IgE-FA share several pathophysiologic features, including epithelial barrier dysfunction, innate and adaptive immune abnormalities, and microbial dysbiosis, which may be critical for the clinical progression between these diseases. Revolutionary advances in targeted biologic therapies have demonstrated the benefit of inhibiting type 2 immune responses, using dupilumab (anti-IL-4Rα) or omalizumab (anti-IgE), to potentially reduce symptom burden for both diseases in pediatric populations. While the potential for biologics to promote disease remission (AD) or sustained unresponsiveness (IgE-FA) remains unclear, the refinement of biomarkers to predict infants at risk for atopic disorders provides promise for prevention through timely intervention.

CONCLUSION

AD and IgE-FA exhibit common features that may be leveraged to develop biologic therapeutic strategies to treat both conditions and even prevent atopic progression. Future studies should be designed with consistent age-stratification in the pediatric population and standardized regimens of adjuvant oral immunotherapy or dose-escalation (IgE-FA) to improve cross-study interpretation.

7

¿Rinitis alérgica (RA) sin IgE? No te olvides de la RA local

Local Allergic Rhinitis

Paloma Campo, Giorgio Walter Canonica

J Allergy Clin Immunol Pract . 2024 Jun;12(6):1430-1433

ABSTRACT

Local allergic rhinitis (LAR) is defined by a clinical history suggestive of allergic rhinitis (AR), negativity of systemic IgE measurement and positive response to nasal allergen challenge (NAC). The term local respiratory allergy includes LAR, local allergic asthma (positive response in bronchial allergen challenge) and dual allergic rhinitis defined by the coexistence of AR and LAR. LAR worsens in severity and presence of comorbidities over time, and it is an independent entity from AR. Prevalence is higher in Mediterranean countries. LAR onset occurs during childhood in 36% of cases. Physiopathological features of LAR are: increased nasal eosinophilic inflammation, tryptase and eosinophil cationic protein, and presence of nasal specific IgE in secretions of 20-40% of subjects. A recent study demonstrated increase in sequential class switch recombination to IgE markers in mucosa of LAR with accumulation of IgE+ CD38+ plasmablasts. Moreover, there is increased expression in B cells of mucosal homing receptors CXCR3+ and CXCR4 in peripheral blood, with accumulation of Th9 and Th2 cells. NAC is the gold standard in the diagnosis of LAR. The measurement of specific IgE in nasal secretions basophil activation test or are still not suitable for diagnosis. There is ample evidence of the usefulness of allergen immunotherapy in the treatment in LAR after 4 DBPCRT in 152 patients. In conclusion, knowledge about LAR is continuously increasing, with detailed definition of physiopathological mechanisms and new phenotypes. More awareness of the disease should be promoted among different specialists, and NAC must be considered an essential diagnostic tool in any age group, including children.

8

Falta evidencia para recomendar ITA en el síndrome polen-frutas

The effect of subcutaneous and sublingual birch pollen immunotherapy on birch pollen-related food allergy: a systematic review

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Front Allergy . 2024 Jun 6:5:1360073

BACKGROUND

Birch pollen-related food allergy (BPFA) is the most common type of food allergy in birch-endemic areas such as Western and Central Europe. Currently, there is no treatment available for BPFA. Due to the cross-reactivity between birch pollen and a range of implicated plant foods, birch pollen allergen immunotherapy (AIT) may be effective in the treatment of BPFA. In this study, we systematically evaluate the effectiveness of birch pollen specific subcutaneous or sublingual immunotherapy in treating BPFA.

METHODS

A search was performed in the PubMed, Embase, and Cochrane libraries. Studies were independently screened by two reviewers against predefined eligibility criteria. The outcomes of interest were changes in (1) severity of symptoms during food challenge, (2) eliciting dose (ED), and (3) food allergy quality of life (FA-QoL). The validity of the selected articles was assessed using the revised Cochrane risk of bias tool. We focused on studies with the lowest risk of bias and considered studies with a high risk of bias as supportive. Data were descriptively summarized.

RESULTS

Ten studies were selected that included 475 patients in total. Seven studies were categorized into "high risk of bias" and three into "moderate risk of bias." The three moderate risk of bias studies, with a total of 98 patients, reported on severity of symptoms during challenge and on the ED. All three studies had a control group. Compared to the control group, improvement in severity of symptoms was observed during challenge in two out of the three studies and on the eliciting dose in one out of three. Only one study investigated the effect of birch pollen AIT on FA-QoL, showing that there was no significant difference between patients receiving subcutaneous immunotherapy or a placebo. Of the seven supportive studies, four had a control group and of those, three showed improvement on both severity of symptoms and ED. None of the supportive studies investigated the effect of the therapy on FA-QoL.

CONCLUSION

This systematic review shows that there is not enough evidence to draw firm conclusions about the effect of AIT on BPFA. Future research is warranted that uses robust clinical studies that include long-term effects, QoL, and multiple BPFA related foods.

9

Perdamos el miedo a mezclar

Efficacy and safety of subcutaneous immunotherapy with polymerized allergen mixtures in polyallergic patients. ARES observational study

Marcela Santaolalla, José Arias-Irigoyen, Jose Miguel Soler, José María Duque, Rosario Escudero, José Luis Pérez-Formoso et al

Expert Rev Clin Immunol . 2024 Jun 27. doi: 10.1080/1744666X.2024.2373886

BACKGROUND

Administration of allergen mixtures of many components comprises the most common approach for American allergists regarding the management of polyallergic patients. European allergists, however, are more reluctant to this type of treatment due to thepotential drawbacks of mixing extracts.

RESEARCH DESIGN AND METHODS

To assess the efficacy and safety of subcutaneous immunotherapy (SCIT) with polymerizedallergen mixtures without dilutional effect in polyallergic patients.Thisobservational, prospective, multicenter study included patients (between 5- 60 years) with respiratory allergic diseases that had been prescribed with SCITwith mixtures of two pollen or mite extracts. Changesin Symptoms and Medication Score (SMS) and in rhinitis quality of life questionnaire (RQLQ), subjective clinicalimprovement, treatment satisfaction and tolerability were assessed after the1-year treatment.

RESULTS

115 patients were included in the assessment. Mean global SMS decreased from 3.5 (SD = 1.1) to1.6 (SD = 1.2) points, with a meanabsolute reduction of 1.6 (SD = 1.3) points in the RQLQ score ($p < 0.001$, Wilcoxon test). General subjective clinical improvements anda good treatment satisfaction and tolerability were observed.

CONCLUSION

SCIT with polymerizedallergen mixtures from either pollen or mite extracts proved to be an effectiveand safe treatment option for polyallergic patients suffering from allergicrespiratory diseases.

10

No todo es IgE en la alergia a alimentos

Allergen-specific IgA and IgG antibodies as inhibitors of mast cell function in food allergy

Furiness KN, El Ansari Y, Oettgen HC, Kanagaratham C.

Front Allergy. 2024 Jun 11:5:1389669

ABSTRACT

Food allergy, a group of adverse immune responses to normally innocuous food protein antigens, is an increasingly prevalent public health issue. The most common form is IgE-mediated food allergy in which food antigen-induced crosslinking of the high-affinity IgE-receptor, FcεRI, on the surface of mast cells triggers the release of inflammatory mediators that contribute to a wide range of clinical manifestations, including systemic anaphylaxis. Mast cells also play a critical function in adaptive immunity to foods, acting as adjuvants for food-antigen driven Th2 cell responses. While the diagnosis and treatment of food allergy has improved in recent years, no curative treatments are currently available. However, there is emerging evidence to suggest that both allergen-specific IgA and IgG antibodies can counter the activating effects of IgE antibodies on mast cells. Most notably, both antigen-specific IgA and IgG antibodies are induced in the course of oral immunotherapy. In this review, we highlight the role of mast cells in food allergy, both as inducers of immediate hypersensitivity reactions and as adjuvants for type 2 adaptive immune responses. Furthermore, we summarize current understanding of the immunomodulatory effects of antigen-specific IgA and IgG antibodies on IgE-induced mast cell activation and effector function. A more comprehensive understanding of the regulatory role of IgA and IgG in food allergy may provide insights into physiologic regulation of immune responses to ingested antigens and could seed novel strategies to treat allergic disease.

1

El secreto está en la B. La ITO consigue una respuesta de células B similar a la remisión natural.

Allergen-specific B cell responses in oral immunotherapy-induced desensitization, remission, and natural outgrowth in cow's milk allergy.

Satitsuksanoa P, van de Veen W, Tan G, Lopez JF, Wirz O, et al

Allergy. 2024 Jul 11. doi: 10.1111/all.16220. Epub ahead of print. PMID: 38989779.

BACKGROUND

Antigen-specific memory B cells play a key role in the induction of desensitization and remission to food allergens in oral immunotherapy and in the development of natural tolerance (NT). Here, we characterized milk allergen Bos d 9-specific B cells in oral allergen-specific immunotherapy (OIT) and in children spontaneously outgrowing cow's milk allergy (CMA) due to NT.

METHODS

Samples from children with CMA who received oral OIT (before, during, and after), children who naturally outgrew CMA (NT), and healthy individuals were received from Stanford biobank. Bos d 9-specific B cells were isolated by flow cytometry and RNA-sequencing was performed. Protein profile of Bos d 9-specific B cells was analyzed by proximity extension assay.

RESULTS

Increased frequencies of circulating milk allergen Bos d 9-specific B cells were observed after OIT and NT. Milk-desensitized subjects showed the partial acquisition of phenotypic features of remission, suggesting that desensitization is an earlier stage of remission. Within these most significantly expressed genes, IL10RA and TGFB3 were highly expressed in desensitized OIT patients. In both the remission and desensitized groups, B cell activation-, Breg cells-, BCR signaling-, and differentiation-related genes were upregulated. In NT, pathways associated with innate immunity characteristics, development of marginal zone B cells, and a more established suppressor function of B cells prevail that may play a role in long-term tolerance. The analyses of immunoglobulin heavy chain genes in specific B cells demonstrated that IgG2 in desensitization, IgG1, IgA1, IgA2, IgG4, and IgD in remission, and IgD in NT were predominating. Secreted proteins from allergenspecific B cells revealed higher levels of regulatory cytokines, IL-10, and TGF-β after OIT and NT.

CONCLUSION

Allergen-specific B cells are essential elements in regulating food allergy towards remission in OIT-received and naturally resolved individuals.

2

¿Vacunar RL extensa tras picadura de insecto o no vacunar? Esa es la cuestión.

Should patients with a large local reaction be offered VIT? A Pro-Con debate.

Bilò MB, Golden DBK, Braschi MC, Martini M

J Allergy Clin Immunol Pract. 2024 Jul 5:S2213-2198(24)00685-8. doi: 10.1016/j.jaip.2024.06.043. Epub ahead of print. PMID: 38972507.

ABSTRACT

Insect stings can cause large local reactions (LLRs) that are IgE-mediated and associated with considerable morbidity. A risk for systemic reactions including anaphylaxis to subsequent stings has been reported and is often noted by patients and health care providers. Guidelines do not recommend venom immunotherapy (VIT) for LLR based on the relatively low risk of anaphylaxis, but this is debated in this review. On the Pro side: the risk of anaphylaxis may be higher than reported in the limited literature, especially in patients who had only 1 LLR; new species with more potent stings are spreading into new areas; the quality of life can be markedly impaired by LLR; VIT is generally safe and highly effective. On the Con side: LLR are benign; stings occur infrequently; VIT has significant cost; systemic reactions occur more often to VIT than to stings in patients with LLR; FDA approval and published guidelines do not recommend VIT for LLR. In practice, shared decision-making is appropriate to incorporate knowledge of the natural history and known high-risk factors in the context of the patient's personal values and preferences.

3

¡No esperes 3 años, biomarcadores de efectividad a los 2-4 meses del inicio de ITA!

A recent patent in allergy & immunology: Biomarkers on allergen-specific memory B cells to predict allergen immunotherapy outcome.

van Zelm MC, O'Hehir RE, McKenzie CI

Allergy. 2024 Aug;79(8):2295-2297. doi: 10.1111/all.16238. Epub 2024 Jul 9. PMID: 38979794.

4

La ITA con comprimidos de árboles es segura y efectiva.

Treatment with the SQ tree sublingual immunotherapy tablet is safe and well tolerated in real-life.

Pfaar O, Wolf H, Reiber R, Knulst A, Sidenius K, et al
Clin Transl Allergy. 2024 Jul;14(7):e12373. doi: 10.1002/clt2.12373. PMID: 38956447; PMCID: PMC11219271.

BACKGROUND
The SQ tree sublingual immunotherapy (SLIT) tablet is authorised for treatment of allergic rhinoconjunctivitis with or without asthma in trees of the birch homologous group in 21 European countries. The primary objective of this study was to explore the safety in real-life.

METHODS
In a prospective, non-interventional post authorisation safety study (EUPAS31470), adverse events (AEs) and adverse drug reactions (ADRs) at first administration and follow-up visits, symptoms, medication use, and pollen food syndrome were recorded by physicians in 6 European countries during the first 4-6 months of treatment.

RESULTS
ADRs with the SQ tree SLIT-tablet were reported in 57.7% of 1069 total patients (median age 36.0 years, 53.7% female) during the entire observation period (severity, mild-to moderate: 70.1%, severe: 4.7%, serious: 0.7%) and in 45.9% after first administration. ADRs were not increased with pollen exposure at first administration. With coadministration of the SQ tree and grass SLIT-tablet AEs were reported in 73.8% of patients and in 52.8% with the SQ tree SLIT-tablet alone. Nasal and eye symptoms improved in 86.9% and 80.9% of patients and use of symptomatic medication in 76.0%. PFS with symptoms was reported in 43.0% of patients at baseline and in 4.3% at the individual last visit.

CONCLUSIONS
The results of this non-interventional safety study with the SQ tree SLIT-tablet confirm the safety profile from placebo-controlled clinical trials and support effectiveness in real-life according to the published efficacy data. Safety was not impaired by pollen exposure at first administration or co administration with other SLIT-tablets.

5

¿Qué son los nanoanticuerpos y cuál es su utilidad en alergología?

Single-Domain Antibodies-Novel Tools to Study and Treat Allergies.

Zettl I, Bauernfeind C, Kollárová J, Flicker S
Int J Mol Sci. 2024 Jul 11;25(14):7602. doi: 10.3390/ijms25147602. PMID: 39062843; PMCID: PMC11277559.

ABSTRACT
IgE-mediated allergies represent a major health problem in the modern world. Apart from allergen-specific immunotherapy (AIT), the only disease-modifying treatment, researchers focus on biologics that target different key molecules such as allergens, IgE, or type 2 cytokines to ameliorate allergic symptoms. Singledomain antibodies, or nanobodies, are the newcomers in biotherapeutics, and their huge potential is being investigated in various research fields since their discovery 30 years ago. While they are dominantly applied for theranostics of cancer and treatment of infectious diseases, nanobodies have become increasingly substantial in allergology over the last decade. In this review, we discuss the prerequisites that we consider to be important for generating useful nanobody-based drug candidates for treating allergies. We further summarize the available research data on nanobodies used as allergen monitoring and detection probes and for therapeutic approaches. We reflect on the limitations that have to be addressed during the development process, such as in vivo half-life and immunogenicity. Finally, we speculate about novel application formats for allergy treatment that might be available in the future.

6

Efecto de la ITA con ácaros según las bases de datos de prescripción.

House dust mite immunotherapy: A real-world, prescription data-based analysis.

Mösges R, Richter H, Sager A, Weber J, Müller T
Clin Transl Allergy. 2024 Jul;14(7):e12382. doi: 10.1002/clt2.12382. PMID: 38988207; PMCID: PMC11237338.

BACKGROUND
House dust mite (HDM) sensitisation can contribute to the development of allergic rhinoconjunctivitis (AR) or allergic asthma (AA). As treatment, allergen immunotherapy (AIT) is a promising approach, since it aims building immunotolerance against allergens, therewith establishing longterm efficacy. The evaluation of AIT has been investigated in many randomised controlled trials, whereas few real-world evidence studies are available.

METHODS
We used data from the longitudinal prescription data base IQVIA LRx. Data on initial AIT prescriptions against HDM from January 2009 to December 2013 was analysed regarding treatment (subcutaneous AIT with either depigmented polymerised allergen extract [dSCIT] or other allergens [oSCIT], or sublingual immunotherapy [SLIT]) and treatment duration. Treatment groups were compared with a control group of AR patients not receiving AIT. Data on symptomatic medication was collected until February 2017 and progression of AR and AA was compared.

RESULTS
Data of 7260 patients with AIT prescriptions and of 21,780 control patients was analysed. AIT was associated with a significant decrease of AR medication intake compared with control (dSCIT: -34.0%, $p < 0.0001$; oSCIT: -25.7%, $p < 0.0001$; SLIT: -37.7%, $p = 0.0026$). In asthmatics, SCIT was associated with a significant decrease of asthma medication compared with control (dSCIT: -45.2%, $p < 0.0001$; oSCIT: -32.9%, $p < 0.0001$). Further, a significantly reduced likelihood for onset of asthma medication was demonstrated in patients treated with SCIT compared with controls (dSCIT OR: 0.759, $p = 0.0476$; oSCIT OR: 0.815, $p = 0.0339$).

CONCLUSION
Real-world data analyses indicate that AIT, particularly given via a subcutaneous route, reduces the need of medication against AR and AA and might delay the onset of asthma medication in patients with AR.

7

Confirmado, las tabletas (300IR) frente a ácaros son universalmente seguras.

Safety of 300IR house dust mite sublingual tablet from pooled clinical trial and post-marketing data.

Worm M, Demoly P, Okamoto Y, Vidal C, Daghildjian K, Yan K, Casale TB, Bergmann KC

World Allergy Organ J. 2024 Jun 25;17(7):100924. doi: 10.1016/j.waojou.2024.100924. PMID: 39035788; PMCID: PMC11259958.

BACKGROUND

The 300IR house dust mite (HDM) sublingual immunotherapy (SLIT) tablet is approved for treatment of HDM-induced allergic rhinitis (AR). To provide a comprehensive review of the 300IR HDM-SLIT tablet safety profile based on randomized controlled trial (RCT) pooled data and postmarketing (PM) pharmacovigilance data.

METHODS

Subjects (5-65 years) with confirmed HDM-AR with or without controlled asthma were treated with 300IR or placebo in 8 RCTs. Reported treatment-emergent adverse events (TEAEs) were pooled and analyzed descriptively in subsets of adults/adolescents and children. Adverse reactions (ADRs) collected from spontaneous reporting and PM studies through a pharmacovigilance system since the first marketing authorization were also analyzed.

RESULTS

Across RCTs, 1853 subjects were treated with the 300IR HDM-SLIT tablet and 1846 with placebo. In both subsets of adults/adolescents and children whichever their asthma status, treatment-related TEAEs of higher incidence in active groups vs placebo were mostly consistent with mild or moderate local application-site reactions. They were mainly reported on the first days of treatment and decreased over time. 4 severe laryngopharyngeal reactions (2 requiring adrenaline/epinephrine) and 1 moderate eczema considered serious rapidly resolved with medications; no anaphylaxis was reported. In PM settings, ADRs reported in more than 235,000 patients were in line with RCT findings. Severe systemic reactions occurred rarely; 12 anaphylactic reactions resolved safely (5 with adrenaline). No new safety signal was raised.

CONCLUSION

Safety data from RCTs and more than 7 years of real-life experience confirmed the favorable safety profile of 300IR HDM-SLIT tablet in patients across different regions, regardless of age and asthma status.

8

¿El diagnóstico molecular puede sustituir a la provocación oral en la alergia a alimentos?

Is Component-Specific Antibody Testing Sufficient to Replace the Oral Food Challenge in the Diagnostics of PeanutSensitized Children? A Proof-of-Concept Study.

Łyżwa K, Prasek K, Krupa-Łaska A, Zielińska J, Krejner-Bienias A, et al

Int J Mol Sci. 2024 Jul 6;25(13):7415. doi: 10.3390/ijms25137415. PMID: 39000522; PMCID: PMC11242119.

ABSTRACT

1) Peanut allergy is associated with high risk of anaphylaxis which could be prevented by oral immunotherapy. Patients eligible for immunotherapy are selected on the basis of a food challenge, although currently the assessment of antibodies against main peanut molecules (Ara h 1, 2, 3 and 6) is thought to be another option. 2) The current study assessed the relationship between the mentioned antibodies, challenge outcomes, skin tests and some other parameters in peanut-sensitized children. It involved 74 children, divided into two groups, based on their response to a food challenge. 3) Both groups differed in results of skin tests, levels of component specific antibodies and peanut exposure history. The antibody levels were then used to calculate thresholds for prediction of challenge results or symptom severity. While the antibody-based challenge prediction revealed statistical significance, it failed in cases of severe symptoms. Furthermore, no significant correlation was observed between antibody levels, symptom-eliciting doses and the risk of severe anaphylaxis. Although in some patients it could result from interference with IgG4, the latter would not be a universal explanation of this phenomenon. 4) Despite some limitations, antibody-based screening may be an alternative to the food challenge, although its clinical relevance still requires further studies.

9

Pauta de 1 día con ITA frente a melocotón.

Ultrafast regimen for Pru p3 sublingual immunotherapy (SLIT-Peach®) in patients with anaphylactic LTP-Syndrome.

Zamarro Parra MS, Petryk Petryk Y, Carbonell Zamoran J, Carbonell Martinez A

Eur Ann Allergy Clin Immunol. 2024 Jul;56(4):183-187. doi: 10.23822/EurAnnACI.1764-1489.285. Epub 2023 Feb 14. PMID: 36786331.

ABSTRACT

Sublingual immunotherapy with Pru p3 extract (SLIT peach®) is used in allergy patients to multiple plant foods to induce tolerance to nonspecific lipid transfer proteins (nsLTP). The aim of this paper is to communicate the efficacy of a new ultrafast regimen. Until now on the initiation regimen lasts four days. We present a number of 22 patients with LTP-syndrome due to ingestion of different vegetable foods sensitized to Pru p3. According to European Academy of Allergy position paper (1) food immunotherapy is indicated when avoidance measures are ineffective, undesirable, or cause serious limitations on patients quality of life. Our patients had an impact on their quality of life (score > 130) before SLIT measured with (2) EuroPrevall Food Allergy Quality of Life Questionnaire (FAQLQ). The ultrafast regimen in one day is achieved in the 95% of our patients. Mild adverse reactions were observed, such as oral pruritus presence in almost all patients. Only one patient (5%) achieved the maintenance dose in two days due to intense oral pruritus. No patients presented systemic reactions. The maintenance dose achieved consists of 4 drops (0,16 ml) from vial number 4 daily. The concentration of Pru p3 in vial nº4 is 50 cg/ml. Four drops a day equals 8 micrograms of Pru p3. This new ultrafast regimen in one day is secure in patients with LTP Syndrome to induce tolerance to SLIT-peach® (Pru p3 extract).

10

¿Qué no era para infantes? Resultados de SLIT frente a ácaros en menores 5 años.

Efficacy and safety of sublingual immunotherapy using house dust mite tablet for 1-4 years old children with perennial allergic rhinitis.

Sasamoto K, Nagakura KI, Asaumi T, Fusayasu N, Ohashi-Doi K, Yanagida N, Sato S, Ebisawa M

Pediatr Allergy Immunol. 2024 Jul;35(7):e14203. doi: 10.1111/pai.14203. PMID: 39045695.

BACKGROUND

Sublingual immunotherapy (SLIT) for perennial allergic rhinitis (AR) has not been extensively studied in preschoolers. We investigated the efficacy and safety of house dust mite (HDM) SLIT-tablet for children aged 1-4 years.

METHODS

Children aged 1-4 years with AR were divided into SLIT (n = 22) and control (n = 12) groups based on their guardians' preferences. The SLIT group received a daily dose of 10,000 JAU of HDM SLIT tablet for 12 months, whereas the control group received symptomatic treatment only.

RESULTS

The baseline median age was 41 and 34 months in the SLIT and control groups, respectively, and the median AR symptom score was 4 for both groups. Compared with baseline, the AR symptom score had decreased significantly in the SLIT group after 12 months (score: 3, p = .002), whereas it tended to increase in the control group (score: 6, p = .08). Adverse reactions to SLIT were mild and occurred in eight patients (36%). In the SLIT group, Dermatophagoides (D.) farinae-specific IgE (sIgE) levels increased during the first 6 months and decreased to baseline levels at 12 months. In the control group, D. farinae-sIgE levels had increased significantly at 12 months compared to baseline (p = .01). D. farinae specific IgG4 and HDM IgE-blocking factor levels were significantly increased at 12 months compared to baseline in the SLIT group only (p < .001). A lower wheezing frequency was seen in the SLIT group (0.3%) compared to the control group (0.7%).

CONCLUSION

This pilot study demonstrated the efficacy, safety, and immunomodulatory effects of HDM SLIT-tablet in preschoolers with AR.

BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Agosto 2024

1

Mejor prevenir que curar, ¡prescribe ITA!

Preventive allergen immunotherapy with inhalant allergens in children.

Varsha Dwivedi, Sonja Kopanja, Klara Schmidthaler, Justyna Sieber, Christina Bannert, Zsolt Szépfalusi

Allergy. 2024 Aug;79(8):2065-2087. doi: 10.1111/all.16115.

ABSTRACT

The efficacy and safety of preventive allergen immunotherapy (pAIT) in children are currently under investigation. Here, we provide an overview of pAIT with respiratory allergens concerning the prevention of new sensitizations, allergic disease onset and progression as well as further immunomodulatory effects. Three databases were searched for clinical pAIT studies in children. Selected publications were reviewed for preventive outcomes according to prevention level (primary, secondary, and tertiary), allergen type, administration route, dose, and treatment duration. The primary prevention approach appears safe but showed no allergen-specific effect on new sensitizations. Secondary prevention seems feasible and may induce regulatory T cell-mediated immunotolerance. The number of studies at these prevention levels is limited. Tertiary prevention with grass and/or tree pollen-based pAIT has shown efficacy in preventing disease progression from allergic rhinitis/conjunctivitis to asthma. Data on tertiary pAIT with house dust mites and other allergen types are inconclusive. Subcutaneous and sublingual routes appear similarly effective, but head-to-head comparative paediatric studies are scarce. Additionally, there are fewer placebo-controlled studies. Nevertheless, immunomodulatory outcomes of pAIT are encouraging. Currently, limited but favourably suggestive evidence is available for preventing respiratory allergic diseases in children by pAIT. Primary and secondary prevention have potential and warrant further investigation through well-designed studies.

2

Cómo diagnostico y qué hago con los alérgicos a himenópteros y mastocitosis.

Mast cell disorders and Hymenoptera venom-triggered anaphylaxis: evaluation and management.

Nathan A Boggs, Ilaria Tanasi, Karin Hartmann, Roberta Zanotti, David Gonzalez-de-Olano

J Allergy Clin Immunol Pract. 2024 Aug 24:S2213-2198(24)00853-5. doi: 10.1016/j.jaip.2024.08.034.

ABSTRACT

Patients with Hymenoptera venom allergy (HVA), especially those with severe anaphylaxis, frequently have concomitant clonal mast cell disease (MCD) in the form of systemic mastocytosis or monoclonal mast cell activation syndrome. Detection of clonal MCD is important since it will have significant consequences for management of HVA. Therefore, we recommend patients with HVA be systematically screened for clonal MCD. The pre-test probability of clonal MCD can be assessed in a stepwise fashion starting with examination of the skin for typical monomorphic maculopapular cutaneous mastocytosis (MPCM) lesions; measurement of the baseline serum tryptase (BST) and tryptase genotyping for patients with BST>11 ng/mL; followed by the REMA score which is calculated by utilizing anaphylaxis clinical features, BST, and patient sex. A bone marrow biopsy should be performed in patients with monomorphic MPCM, a REMA score ≥2, or an elevated BST based upon tryptase genotype. Patients with HVA and a clonal MCD should be treated with immunotherapy directed against the Hymenoptera venom for which they are sensitized. For this high-risk subgroup of HVA patients, it is recommended to continue immunotherapy for more than 5 years or indefinitely and to carry at least three epinephrine autoinjectors. Future studies should determine whether KIT D816V-selective tyrosine kinase inhibitors are effective at preventing or reducing severity of Hymenoptera-venom triggered anaphylaxis in patients with clonal MCD.

3

Factores de riesgo vigentes en alergia a himenópteros.

Risk factors for severe sting reactions and side effects during venom immunotherapy.

Gunter J Sturm, Eva Schadelbauer, Giorgia Marta, Patrizia Bonadonna, Mitja Kosnik

J Allergy Clin Immunol Pract. 2024 Aug 20:S2213-2198(24)00845-6. doi: 10.1016/j.jaip.2024.08.025.

ABSTRACT

Understanding the risk factors leading to severe systemic sting reactions (SSR) is crucial for initiating venom immunotherapy (VIT) and for educating affected individuals and their families. Some of these risk factors are well-established, some are no longer considered risk factors, and some remain controversial. Well-established risk factors for severe SSR include clonal mast cell disease, high baseline serum tryptase, and advanced age. The absence of skin symptoms and the rapid onset of symptoms are indicators of severe SSR. Recent publications indicate that antihypertensive treatment and stings in the head and neck area are not risk factors for severe SSR. VIT is the only available treatment that can potentially prevent further anaphylactic reactions. Although rare and generally manageable, individuals undergoing VIT may experience systemic adverse events (sAE). More sAE are expected in patients undergoing bee VIT compared to vespid VIT. The role of elevated baseline serum tryptase as a risk factor for sAE remains debated, but if it is a factor, the risk is increased by only about 1.5-fold. Rapid up-dosing protocols, depending on the specific regimen, can also be associated with more sAE. Severe initial SSR, antihypertensive medication, high skin test reactivity, and high specific IgE levels are not risk factors for sAE.

4

Aprendamos de la evidencia para evitar efectos adversos con la ITA.

Allergen immunotherapy adverse events in adults with respiratory allergies-data from ADER: An EAACI task force report.

Asllani Julijana, Mitsias Dimitrios, Konstantinou George, Qirko Etleva, Hitaj Mirela, Musollari Sybi et al

Allergy. 2024 Aug 22. doi: 10.1111/all.16286.

BACKGROUND

Registries can yield important insights on allergen immunotherapy (AIT) outcomes in daily clinical practice. However, systematic recordings of adverse events (AE) due to AIT in real-life are lacking.

METHODS

The Allergen Immunotherapy Adverse Events Registry (ADER) is a prospective, multicenter registry on real life AIT safety. Data on adults (>18 years old) with respiratory allergies receiving AIT with mites, pollens, epithelia, and/or molds were retrieved and analyzed from ADER. The frequency, characteristics and risk factors of AE were investigated. The MedDRA terminology was used to record AE.

RESULTS

A total of 1545 individuals with a mean age of 33 ± 10 years receiving 1815 AIT courses (n = 1060 sublingual (SLIT); n = 755 subcutaneous (SCIT)) in centers from eight countries were included. Patients had allergic rhinitis (65%) or, asthma only (3.7%) or rhinitis with asthma (31.2%). Grass was the most frequent specific sensitizer (60.7%), followed by mites (45.5%), birch pollen (20.6%), epithelia (16.1%), and molds (8%). There were 296 AE recorded in 115 patients (7.4%). A higher frequency of AE occurred during up-dosing (59%) compared to maintenance. Severe reactions were rare (0.2%), all in the context of SCIT. After 6 weeks of maintenance only one moderate AE was recorded. The most frequently reported symptoms were from the respiratory system and the skin. Having asthma, doing SCIT, AIT with mugwort, cat, or birch were associated with higher risk for AE while the use of allergoids induced lower risk.

CONCLUSION

In real life clinical practice, AIT-associated AE occur in a minority of patients, while severe reactions are rare. The presence of asthma and use of SCIT are risk factors, while the use of modified allergens lowers the risk.

5

Estudios de “vida real” aplicados a ITA: ¿mejorarán los resultados?

RIAIT (Italian Registry of Allergen Immunotherapy): Protocol for a New Tool in a New Vision of DiseaseModifying Therapy for Allergists.

Giovanni Costanzo, Cristiano Caruso, Giovanni Paoletti, Ilaria Baglivo, Stefania Colantuono, Diego Bagnasco

J Pers Med. 2024 Aug 12;14(8):854. doi: 10.3390/jpm14080854.

ABSTRACT

Randomized controlled trials have demonstrated responses to clinical parameters, but a significant proportion of allergy patients in reallife settings would have been excluded from such studies. Therefore, real world research is needed, and there is a growing body of information on allergen immunotherapy's long-term effectiveness and safety. Real-world evidence can be a valuable instrument to better understand the patient's journey and the effectiveness and safety of therapies. For this purpose, a registry will be used for the first time in Italy to evaluate the impact of allergen immunotherapy on several outcomes, including quality of life and disease related effects in the pediatric and adult allergic population with a socio economic assessment and respect to real-world health.

6

Tener un perfil T2 es un factor de riesgo para presentar reacciones con la ITA.

Augmented type 2 inflammatory response in allergic rhinitis patients experiencing systemic reactions to house dust mite subcutaneous immunotherapy.

Ping Ji, Lin Yang, Li Zhu, Lintao Hu, Yin Wang, Cancan Shi et al

Pediatr Allergy Immunol. 2024 Aug;35(8):e14207. doi: 10.1111/pai.14207.

BACKGROUND

Subcutaneous immunotherapy (SCIT) can induce systemic reactions (SRs) in certain patients, but the underlying mechanisms remain to be fully elucidated.

METHODS

AR patients who were undergoing standardized HDM SCIT (Alutard, ALK) between 2018 and 2022 were screened. Those who experienced two consecutive SRs were included in the study group. A control group was established, matched 1:1 by gender, age, and disease duration with the study group, who did not experience SRs during SCIT. Clinical and immunological parameters were recorded and analyzed both before SCIT and after 1 year of treatment.

RESULTS

A total of 161 patients were included, with 79 (49.07%) in the study group. The study group had a higher proportion of AR combined asthma (26.8% vs. 51.8%, $p < 0.001$) and higher levels of sIgE to HDM and HDM components (all $p < .001$). Serum IL-4 and IL-13 levels in the study group were higher than those in the control group ($p < .05$). The study group received a lower maintenance dosage of HDM extracts injections than control group due to SRs (50000SQ vs. 100000SQ, $p < .05$). After 1 year of SCIT, the VAS score, the lung function parameters of asthmatic patients over 14 years old significantly improved in both groups (all $p < .05$). After a 7-day exposure to 20 μg/mL HDM extracts, the percentages of Th1, Th17, Tfh10, and Th17.1 in PBMCs decreased, while the Tfh13 cells significantly increased in the study group ($p < .05$).

CONCLUSION

The type 2 inflammatory response is augmented in HDM-induced AR patients who experienced SRs during SCIT. Despite this, SCIT remains effective in these patients when administered with low-dosage allergen extracts.

7

Subcutánea y sublingual, ambas efectivas en asma infantil.

Efficacy and safety of subcutaneous and sublingual allergen immunotherapy in the treatment of asthma in children: a systematic review and meta-analysis.

Wenwen Yang, Weijie Wang, Yishu Ji, Huisong Pan

J Asthma. 2024 Aug 28:1-10. doi: 10.1080/02770903.2024.2391441.

OBJECTIVE

Asthma is a common chronic condition in children globally. Allergen-specific immunotherapy, such as subcutaneous (SCIT) and sublingual (SLIT) therapies, are promising by increasing allergen tolerance. This meta-analysis compares the efficacy and safety of SLIT and SCIT in pediatric asthma.

METHODS

We searched PubMed, Cochrane Library, and Embase for randomized controlled trials and case-control studies comparing SLIT and SCIT in asthmatic children. Meta-analysis was conducted using random-effects models with calculations via R software version 4.3.2 and RevMan version 5.4. Study quality and bias risk were assessed using the Newcastle-Ottawa Scale and Cochrane Risk of Bias Tool.

RESULTS

The literature search yielded a total of 1787 records, with 7 studies meeting the inclusion criteria after screening and assessments. There was no significant difference in the Total Asthma Symptoms Score between SLIT and SCIT (mean difference -0.05 [95% CI: -0.21; 0.10]). However, asthma improvement rates were higher in the SLIT group (risk ratio 0.77 [95% CI: 0.64; 0.93]). FEV1 improvement showed no significant difference (mean difference -1.60 [95% CI: -6.27; 3.08]). Adverse events were similar between the treatments (risk ratio 0.56 [95% CI: 0.11; 2.82]).

CONCLUSIONS

SLIT and SCIT were generally similarly effective and safe for treating pediatric asthma. SLIT may be preferred due to its noninvasive administration. More research is needed on long-term effects and tailored treatment approaches.

8

¿Qué extracto comercial de ITA frente a ácaros tiene mejor evidencia?

The evidence for commercial house dust mite immunotherapy products: A pragmatic systematic review with narrative synthesis.

Timothy West, Constance H Katelaris

J Allergy Clin Immunol Glob. 2024 Apr 10;3(3):100255. doi: 10.1016/j.jacig.2024.100255.

ABSTRACT

House dust mite (HDM) allergen immunotherapy (AIT) has an established role in the treatment of perennial allergic rhinitis (AR) and allergic asthma (AA) triggered by HDM sensitization. We aimed to identify all double-blind, randomized, placebo-controlled trials of HDM AIT for the treatment of AR and AA in humans and to summarize the evidence for AIT products that are currently manufactured and available for clinical use. A total of 56 eligible double-blind, randomized, placebo-controlled trials of HDM AIT for the treatment of AA and/or AR in humans fit the inclusion criteria and investigated a total of 14 commercial AIT products; together, the 56 studies enrolled a total of 14,619 patients. Of the 56 studies, 39 studies investigated the current manufacturer-recommended maintenance dose (MRMD) of the product, and 17 investigated other doses. We identified 39 studies (12,539 patients randomized) for 8 sublingual immunotherapy (SLIT) products and 17 studies (2,080 patients randomized) for subcutaneous immunotherapy products. For AR, 3 products, the ALK 12 standardized-quality (SQ-HDM) SLIT tablet, the ALK 6 SQ HDM tablet, and the SG 300 index of reactivity SLIT tablet, had both dose-finding studies (DFSs) and phase III definitive studies (DSs) to demonstrate efficacy of the MRMD of the product. For AA, 2 products, the ALK 12 SQ-HDM SLIT tablet and the ALK 6 SQ-HDM tablet, had both DFSs and DSs for the MRMD. No subcutaneous immunotherapy product had a paired DFS and DS supporting the MRMD. A total of 30 studies of products no longer commercially manufactured were excluded. This study will help to inform clinical care and product selection for the treatment of HDMinduced AR and AA.

9

Los padres que acceden a la ITO buscan la curación.

Real-world adoption of peanut oral immunotherapy in infants and toddlers.

S Shahzad Mustafa, Peter Capucilli, Linh-An Tuong, Denise Sanchez-Tejera, Karthik Vadamalai, Allison Ramsey

J Allergy Clin Immunol Pract. 2024 Aug;12(8):2196-2198.e1. doi: 10.1016/j.jaip.2024.04.043.

ABSTRACT

This study evaluated uptake of infant and toddler, younger than 4 years, peanut oral immunotherapy (POIT), revealing that 67% of families with a peanut-allergic child chose to pursue therapy. The potential for the resolution of peanut allergy was the most cited reason to pursue POIT.

10

Dosis estándar recomendada vs. dosis máxima tolerada.

Individualized sublingual immunotherapy with dynamic maintenance dose ascending for house dust miteinduced allergic rhinitis.

Juan Wang, Ling Cai, Caiqin Huang, Jing Pei, Xinyi Shi, Yuejin Tao

Am J Otolaryngol. 2024 Aug 13;45(6):104476. doi: 10.1016/j.amjoto.2024.104476.

BACKGROUND

Precision dosing in sublingual immunotherapy (SLIT) has become a hotspot gradually, yet no standardized dose adjustment pattern for house dust mite (HDM)-SLIT. This study aims to investigate the clinical feasibility of the dynamic maintenance dose ascending regimen for individualized SLIT.

METHODS

A total of 258 allergic rhinitis (AR) patients treated with HDM-SLIT were included in this retrospective study. Patients were divided into the regular dose (RD) group (n = 101) and the high dose (HD) group (n = 157) according to different maintenance dosages of SLIT. In the RD group, patients received the fixed dose recommended by the manufacturer. In the HD group, patients received a maximum tolerance dose determined by dynamic dose ascending. The clinical efficacy was evaluated by combined symptom and medication score (CSMS) and visual analogue scale score (VAS) at the baseline, 0.5-year, 1-year, and 2-year. The safety was evaluated by adverse events (AEs).

RESULTS

Significant reductions of CSMS and VAS at 0.5 year, 1-year, and 2-year were observed in both the RD group and the HD group compared to the baseline ($P < 0.05$). In addition, greater improvements in these clinical parameters from 0.5- to 2 year were found in the HD group compared to the RD group ($P < 0.05$). For subgroup analysis in the HD group, no significant differences in CSMS and VAS were observed among subgroups of patients <14 years old and patients ≥14 years old ($P > 0.05$). No serious AEs in the two groups and no significant differences were observed between the AE incidence rate of the RD group and HD group during the incremental and maintenance phases.

CONCLUSIONS

The 2-year HDM-SLIT with dynamic maintenance dose ascending regimen offers an "optimal" treatment for AR patients while maintaining safety. This study introduced a pattern for individualized dose adjustment in clinical practice, offering potential benefits for AR patients.

1

"Parecido" no es "igual". La IT es alérgeno-específica

Cross-protection of AIT-induced antibodies to related allergens requires a high degree of structural identity

Demir H, Radauer C, Strobl MR, Scheurer S, Kinaciyan T, Bohle B

Allergy. 2024 Sep 23. doi: 10.1111/all.16323. Epub ahead of print. PMID: 39311416

BACKGROUND

In contrast to sublingual immunotherapy (SLIT) with recombinant Mal d 1 (rMal d 1-SLIT), SLIT with rBet v 1 (rBet v 1-SLIT) induced Mal d 1-cross-reactive antibodies without IgE blocking activity. To elucidate whether the development of cross-protective IgG responses depends on the degree of molecular identity of allergens we compared the cross-reactivity, cross-blocking activity, and affinity of SLIT-induced antibodies with allergens of varying amino acid sequence identities to Bet v 1 and Mal d 1, namely Cor a 1.04 (hazelnut), Pru av 1 (cherry), and Dau c 1 (carrot).

METHODS

Allergen-specific antibodies were quantified by ELISA. IgE blocking was analyzed by inhibition of allergen induced basophil activation and IgE-facilitated allergen-presentation to T cells. The affinity of SLIT-induced antibodies was studied by acidic dissociation ELISA and competition ELISA. Identical surface areas on allergens were predicted using an in-house designed script based on structural alignments.

RESULTS

rBet v 1-SLIT-induced IgG antibodies cross reacted with all allergens except Dau c 1. rMal d 1-SLIT induced antibodies predominantly cross-reacted with Pru av 1 and displayed significantly higher IgE blocking to Pru av 1 than rBet v 1-SLIT-induced antibodies. rMal d 1-SLITinduced IgG1 showed higher affinity to Mal d 1 and Pru av 1. Surface analysis revealed 84% identical area on Mal d 1 and Pru av 1. Furthermore, we identified two surface areas potentially containing epitopes present on these allergens and absent on Bet v 1.

CONCLUSION

In summary, our findings suggest that a relatively high threshold of similarity is required to establish effective cross blocking antibodies to related allergens. Apparently, the structural identity between Bet v 1 and Mal d 1 is below this threshold. Therefore, this study may explain why immunotherapy with birch pollen allergen often fails to reduce birch pollen-related apple allergy.

2

Biomarcadores en desensibilización a alimentos

HLA-DR+ regulatory T cells and IL-10 are associated with success or failure of desensitization outcomes

Zhou X, Dunham D, Sindher SB, Long A, Fernandes A, et al

Allergy. 2024 Sep 18. doi: 10.1111/all.16311. Epub ahead of print. PMID: 39291303

BACKGROUND

Omalizumab (XOLAIR®)-assisted multi-food oral immunotherapy (mOIT) has been shown to safely, effectively, and rapidly desensitize patients with multiple food allergies. In our clinical trial (NCT02626611) on omalizumab-assisted mOIT, different desensitization outcomes (success or failure of desensitization) were observed following a period of either continued or discontinued mOIT. However, the association between the immunological changes induced by omalizumab-assisted mOIT and desensitization outcomes has not yet been fully elucidated. In this study, due to the key roles of regulatory T (Treg) cells and the type 2 helper T cell (Th2) pathway in immune tolerance to food allergens, we aimed to characterize their association with the desensitization outcomes of omalizumab assisted mOIT.

METHODS

Mass cytometry and multiplex cytokine assays were performed on blood samples obtained from participants with allergies to peanut, cashew, or milk in our phase 2 clinical study (NCT02626611). Comprehensive statistical and bioinformatic analyses were conducted on high-dimensional cytometry-based single-cell data and high-throughput multiplex cytokine data.

RESULTS

Our results demonstrated that the frequency of HLA-DR+ Treg cells, and the production of Th2 cytokines (IL-4, IL-5, IL-13, and IL-9) as well as the immunoregulatory cytokine IL-10 by peripheral blood mononuclear cells (PBMCs) was significantly increased in cultures with allergen compared to cultures with media alone at baseline (Week 0). We also observed increased frequency of allergen responsive HLA-DR+ Treg cells and enhanced production of IL-10 by PBMCs in participants who achieved successful desensitization compared to those with failure of desensitization. However, the production of Th2 cytokines by PBMCs did not show significant differences between participants with different desensitization outcomes (success vs. failure of desensitization), despite omalizumab-assisted mOIT inducing a significant reduction in the production of Th2 cytokines.

CONCLUSIONS

We demonstrated that the frequency of HLA DR+ Treg cells and IL-10 cytokine production by PBMCs are associated with desensitization outcomes of omalizumab-assisted mOIT. These findings suggest potential immunological parameters that could be targeted to enhance desensitization success rates.

3

En dermatitis atópica grave, ITA+dupilumab= combinación perfecta

Dupilumab and House Dust Mite Immunotherapy in Patients with Atopic Dermatitis: A Preliminary Study

Bogacz-Piaseczyńska A, Bożek A, Krupka-Olek M, Kawczyk-Krupka A, Zalejska-Fiolka J, Canonica GW

Vaccines (Basel). 2024 Sep 13;12(9):1046. doi: 10.3390/vaccines12091046. PMID: 39340076; PMCID: PMC11435717

BACKGROUND

Severe atopic dermatitis (AD) is a complex disease requiring systemic treatment. This study aimed to assess the effectiveness of combined therapy consisting of dupilumab and sublingual dust mite allergen immunotherapy (SLIT-HDM) in patients with severe AD and HDM allergies.

METHODS

Patients diagnosed with severe AD were included in this randomised, placebo-controlled, double blind 12-month trial; they received SLIT for HDMs and/or dupilumab for 12 months and were compared with patients on cyclosporine. The primary outcomes for the treatment arms were changes in the Eczema Area and Severity Index (EASI), body surface area (%BSA), and Investigator Global Assessment (IsGA) over 12 months. The secondary outcomes were the proportion of patients who achieved IsGA success and reduced medication scores.

RESULTS

Significant improvements were observed in all analysed groups after 12 months of therapy based on the EASI, %BSA, and IsGA. However, the most substantial changes were observed in the groups treated with dupilumab or a combination of SLIT-HDM and dupilumab. Additionally, the proportion of patients who achieved an IsGA reduction was significantly greater in the group receiving combination therapy than in the other groups (9/14 [64% of the group receiving SLIT-HDM] vs. 11/14 [73% of the group receiving dupilumab] vs. 15/17 [88% of the group receiving dupilumab and SLIT-HDM] vs. 7/13 [53% of the group receiving cyclosporine]) ($p < 0.05$).

CONCLUSIONS

In patients with severe AD and HDM allergies, combination treatment with dupilumab and allergen immunotherapy for HDMs may increase the therapeutic benefit over treatment with these methods separately.

4

Se consolida la utilidad de la IT epicutánea frente a cacahuete

Epicutaneous immunotherapy for the treatment of peanut allergy

Ravindran M, Sampson HA, Kim EH, Bee KJ, Green TD, Burks AW

Allergy. 2024 Sep 28. doi: 10.1111/all.16324. Epub ahead of print. PMID: 39340442

ABSTRACT

Peanut allergy treatment options remain limited, but novel approaches are being studied, including epicutaneous immunotherapy (EPIT). EPIT uses the cutaneous immune system to promote tolerance to food allergens. Viaskin Peanut, an approach to EPIT in late-stage clinical development uses an occlusive patch with a condensation chamber that enables natural epidermal water loss to solubilize dry antigen on the patch, which is then absorbed and captured by skin Langerhans cells. This form of EPIT does not require disruption of the skin barrier, thus avoiding a proinflammatory cytokine response by targeting the nonvascularized epidermis and limiting systemic allergen exposure. Extensive preclinical research suggests that Viaskin Peanut has a distinct mechanism of desensitization, including the potential for disease modification, driven by a unique population of regulatory T cells. Numerous clinical studies of Viaskin Peanut have demonstrated desensitization and reductions in reaction severity, particularly in children aged 1 through 11 years, as well as a favorable safety profile with mostly mild-to-moderate skin reactions that were observed to decrease over time. EPIT with Viaskin Peanut may be a potential therapeutic option for peanut allergy that is clinically practical with long-term efficacy and tolerability.

5

La efectividad de la ITA se mide en papel

Evaluation of the Correlation Between Nasal Secretion ECP-MPO Test Papers and Immune Markers in Subcutaneous Immunotherapy of Dust Mites

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J Asthma Allergy. 2024 Sep 11;17:847-862. doi: 10.2147/JAA.S453414. PMID: 39281095; PMCID: PMC11402357

PURPOSE

Up to now, there is no generally accepted biomarker to indicate the clinical response of immunotherapy. This study mainly analyzed the correlation between eosinophil cationic protein myeloperoxidase (ECP-MPO) test papers and other immunotherapy indices in subcutaneous immunotherapy of dust mites and to explore whether the test paper can be used as an auxiliary index to quickly evaluate the efficacy of immunotherapy.

PATIENTS AND METHODS

This study included 53 participants who received subcutaneous immunotherapy at the allergy clinic of Renmin Hospital of Wuhan University and 28 control participants. Six visits were conducted during a prospective study over one year. The results of the ECP-MPO test paper, nasal secretion eosinophil smear and count, nasal secretion ECP concentration, and clinical symptom scores were collected during five follow-up visits after the start of subcutaneous immunotherapy. Th1/Th2/Th17 cytokines, chemokines, IgE, IgG4 against dust mite components, and ECP concentrations were detected in the serum of participants at baseline, six months, and one year after subcutaneous immunotherapy.

RESULTS

The ECP test paper is not only easy to operate, but also can effectively and quickly detect the concentrations of ECP in the nasal secretion and diagnose allergic rhinitis. Symptom score is an important index for evaluating clinical immune efficacy, during subcutaneous immunotherapy, the ECP test paper showed a positive correlation with the symptom score. Simultaneously, during immunotherapy, the changes in the chromogenic grading of the test paper were synchronized with the changes in inflammatory cytokines and eosinophilic chemokines in Th2 cells of serum dust mite IgE. The sIgG4 against dust mites weakly negatively correlated with the concentration of ECP in nasal secretions and the color classification of the ECP test paper.

CONCLUSION

The ECP-MPO test paper has a certain correlation with subcutaneous immunotherapy markers of allergic rhinitis, indicating that the ECP test paper may become an auxiliary biomarker to replace other complex laboratory tests.

6

La ITA también funciona en niños con RAL

Allergen immunotherapy effectivenessin specific nasal reactivity of children with local allergic rhinitis

Loureiro G, Tavares B, Farinha I, Cunha F, Todo-Bom A

Eur Ann Allergy Clin Immunol. 2024 Sep 2. doi: 10.23822/EurAnnACI.1764-1489.358. Epub ahead of print. PMID: 39219549

BACKGROUND

Allergen immunotherapy (AIT) is the only disease-modifying treatment in allergy. Its efficacy has been demonstrated in the treatment of Local Allergic Rhinitis (LAR) in adults. This study intends to evaluate the effectiveness of AIT in specific nasal reactivity of paediatric patients with LAR.

METHODS

Patients diagnosed with LAR to Dermatophagoides pteronyssinus (Dp) were submitted to subcutaneous AIT (SCIT) (depigmented-polymerized Dp allergen extracts) for 3 years. Nasal allergen challenge (NACs) with Dp extract were performed before and 3 years after AIT. NAC response was assessed with peak nasal inspiratory flow (PNIF) and symptom score of Lebel. NACs were considered positive when there was a flow decrease of ≥ 20% in PNIF and a score of symptoms ≥ 3 points. Demographic data and NAC results were analysed.

RESULTS

We included 32 paediatric patients (mean age 9.9±3.08 years, 18 female) and 10 adult patients, (mean age 30.4±12.2 years, 7 female). The symptom score obtained at the 1st minute, 5th minute, 15th minute and 30th minute in response to NAC, were reduced after AIT. The nasal inspiratory flow decrease induced by NAC was also reduced after AIT. This reduction in nasal reactivity was observed in paediatric and in adult patients, both with statistical significance.

CONCLUSIONS

AIT induced a decrease in Dp-nasal specific reactivity in children with LAR. This decline of nasal response to allergen exposure, after AIT treatment, emphasis the interest of this therapeutic approach in LAR, even in paediatric patients.

7

Para la curación con IT, cuanto más joven mejor

Allergic rhinitis in remission with house dust mite subcutaneous immunotherapy

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Asian Pac J Allergy Immunol. 2024 Sep 22. doi: 10.12932/AP-140224-1785. Epub ahead of print. PMID: 39306739

BACKGROUND

House dust mite subcutaneous immunotherapy (HDM SCIT) is a therapeutic option for allergic rhinitis (AR) patients who are unable to properly manage symptoms with standard medications.

OBJECTIVE

This study aimed to determine long-term efficacy and identify predictive factors in the clinical remission of AR patients who completed and discontinued HDM SCIT.

METHODS

This study included 240 AR patients, who completed a three-year course of HDM SCIT at two tertiary hospitals and were currently being discontinued. We followed-up the patients to ask about their current symptoms and allergy medication. Clinical remission was defined by patients who no longer required daily intranasal steroid or oral antihistamine. We compared patients in clinical remission to those still taking medication.

RESULTS

The enrolled patients had a median age of 21.0 (11.0-36.0) years at the time they began HDM SCIT. The clinical remission of AR was achieved in 174 (72.5%) patients. Starting HDM SCIT before the age of 15 and not having asthma were identified as significant and independent predictors of remission (aOR 4.44; 95%CI, 1.72-11.50; p-value 0.002, and 2.67, 95%CI 1.00-7.12; p value 0.049), respectively, as determined by multivariate logistic regression analysis. There were no significant differences in HDM SCIT duration or sensitization patterns between patients in remission and those on medication after discontinuing HDM SCIT for at least one year.

CONCLUSION

HDM SCIT exhibited persistent long-term efficacy after treatment discontinuation. Starting HDM SCIT before the age of 15 and without asthma comorbidity might be predictors of AR remission with HDM SCIT.

8

¿El TAB como predictor de reacción en alergia a alimentos?

A Streamlined Strategy for Basophil Activation Testing in a Multicenter Phase III Clinical Trial

Suárez-Fariñas M, Grishin A, Arif-Lusson R, Bourgoin P, Matthews K, Campbell DE, Busnel JM, Sampson HA

J Allergy Clin Immunol Pract. 2024 Sep 14:S2213-2198(24)00931-0. doi: 10.1016/j.jaip.2024.09.007. Epub ahead of print. PMID: 39284563

BACKGROUND

The basophil activation test (BAT) has been limited to research settings due to technical issues. Novel approaches using dry, ready-to-use reagents and streamlined protocols offer greater flexibility and may open opportunities for easier implementation in clinical research.

OBJECTIVE

Using a streamlined BAT (sBAT) strategy and the settings of the baseline study of the EPITOPE trial of EPicutaneous ImmunoTherapy (EPIT) for peanut allergy, we aimed to assess the feasibility of implementing BAT in a multicenter trial and to evaluate its utility in predicting the outcomes of peanut double-blind placebo-controlled food challenge (DBPCFC).

METHODS

Whole blood samples were collected from subjects aged 1-3 years (n=241) undergoing baseline eligibility DBPCFC in the EPITOPE study across 15 clinical sites in North America. After preparation with sBAT reagents, processed samples were analyzed in a single central laboratory within 5 days of collection and preparation. The eliciting dose (ED) at DBPCFC was determined using PRACTALL criteria. Using a machine learning (ML) approach which incorporated BAT derived features, clinical characteristics, and peanut specific IgE, the ability to predict outcomes of interest (ED [<300 mg or >300 mg] and use of epinephrine) was assessed using data randomly split into training (n=182) and validation (n=59) subsets.

RESULTS

The expression of basophil activation markers CD203c and CD63 correlated with ED and severity outcomes of DBPCFC. Most informative concentrations of peanut extract in the sBAT assay for these associations were 1 and 10 ng/ml. Using ML to assess the ability to predict the outcomes of DBPCFC, the best models using only the BAT-derived features provided relatively high sensitivities of 0.86 and 0.85 for predicting eliciting dose and epinephrine use, respectively, while specificities were lower, ranging from 0.60 to 0.80. While including specific IgE and SPT data in addition to those from sBAT did not improve the ability to identify individuals most at risk for severe reactions, it did improve the ability to identify patients with an eliciting dose above 300 mg.

CONCLUSION

In addition to facilitating implementation in multicenter trials, sBAT retains the potential of BAT to characterize allergic patients and confirms its potential to contribute to predicting the outcome of oral food challenges.

9

La efectividad de la ITA es proporcional al “agotamiento” de las células T

Comparison of Immune Checkpoint Molecule Expression in Different Years of House Dust Mite Subcutaneous Immunotherapy on CD4+ T and Treg Cells in Children with Allergic Rhinitis

Hızlı Demirkale Z, Alpkıray MF, Engin A, Sönmez AD, Yücel E, Tamay Z, Özdemir C, Deniz G, Çetin Aktaş E

Balkan Med J. 2024 Sep 6;41(5):387-395. doi: 10.4274. PMID: 39239953

BACKGROUND

Allergen-specific immunotherapy, a unique inducer of tolerance, may result in T cell exhaution.

AIMS

To investigate how the duration of house dust mite (HDM) subcutaneous immunotherapy (SCIT) affects the expression of major immune checkpoint (ICP) molecules on the surface of CD4+ T-helper and regulatory T (Treg) cells.

STUDY DESING

Cross-sectional study.

METHODS

We enrolled 28 children with HDM-induced allergic rhinitis (AR) and six controls. The study participants were divided into six groups: one group each of patients in their first, second, and third years of HDM-SCIT; one group each comprising those in the first year following HDM-SCIT and those on pharmacotherapy; and the control group. The expression of ICPs on CD4+ T and Treg cells was determined using flow cytometry, and plasma levels of soluble ICPs were estimated by ELISA.

RESULTS

Our results revealed a significant increase in the expression of cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) and lymphocyte activation gene 3 (LAG-3) on CD4+ T cells during the second and third years of SCIT, respectively. Additionally, a strong correlation was observed between the expression of CTLA-4 and T cell immunoglobulin and mucin domain containing molecule 3 in CD4+ T cells. Furthermore, we observed a significant correlation between the expressions of programmed cell death protein-1, CTLA-4, T cell Immunoreceptor with Immunoglobulin and Immunoreceptor Tyrosine-Based Inhbitory Motif domain, and LAG-3 on both CD4+ T and Treg cells. A robust correlation was observed between the plasma levels of soluble ICPs.

CONCLUSION

HDM-SCIT induces CD4+ T cell exhaution, which may contribute to tolerance induction in children with AR.

10

Buscando la mejor opción para una ITSC con alimentos

SubcutaneousImmunotherapy of Food Allergy

Poulsen LK

Curr Allergy Asthma Rep. 2024 Sep 2. doi: 10.1007/s11882-024-01178-2. Epub ahead of print. PMID: 39222196

PURPOSE OF REVIEW

While there are compelling arguments for developing subcutaneous allergen-specific immunotherapy for alleviation of food allergies, there is a limited number of studies in the public domain. The review seeks to present the approaches taken, to explain the paucity of studies, and to identify new roads for development.

RECENT FINDINGS

A literature search revealed clinical trials of immunotherapy of food allergies to fish and peanut, but studies had limited patient numbers, short treatment courses and follow-up periods. Indications, but no clearcut effects, were seen with both classical allergen extracts and hypo-allergenic preparations. A special case is the influence on cross-reactive food allergies, when subcutaneously administered birch-pollen extracts are used for treatment of birch pollen hayfever and/or asthma. Again indications, but no convincing efficacy has been registered. Newer developments include recombinant hypoallergens and DNA-technologies. Subcutaneous immunotherapy for food allergies has not matured to provide clinically relevant treatment opportunities.

BOLETÍN BIBLIOGRÁFICO
DE INMUNOTERAPIA

Octubre 2024

1

Nueva guía de la EAACI sobre alergia a alimentos

EAACI guidelines on the management of IgE-mediated food allergy

Santos AF, Riggioni C, Agache I, Akdis CA, Akdis M, Alvarez-Perea A, Alvaro-Lozano M, Ballmer-Weber B

Allergy. 2024 Oct 30. doi: 10.1111/all.16345. PMID: 39473345

ABSTRACT

This European Academy of Allergy and Clinical Immunology (EAACI) guideline provides recommendations for the management of IgEmediated food allergy and was developed using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach. Following the confirmation of IgE-mediated food allergy diagnosis, allergen avoidance and dietary advice (with support of a specialised dietitian, if possible) together with the provision of a written treatment plan, education on the recognition of allergic symptoms and prescription of medication including adrenaline using an auto-injector are essential. Patients with significant anxiety and requirement for coping strategies may benefit from support from a clinical psychologist. As immunomodulatory interventions, omalizumab is suggested for treatment of IgE-mediated food allergy in children from the age of 1 and adults; and oral allergen-specific immunotherapy is recommended for children and adolescents with peanut allergy and suggested for milk and egg allergies (generally after 4 years of age for milk and egg). Sublingual and epicutaneous immunotherapy are suggested for peanut allergy but are not yet available at the point of care. Future research into disease modifying treatments for IgE mediated food allergy are highly needed, with standardised and patient-focused protocols and outcomes.

2

¿Qué pasa tras finalizar la ITO?

Two-year post-treatment outcomes following peanut oral immunotherapy in the Probiotic and Peanut Oral Immunotherapy-003 Long-Term (PPOIT-003LT) study

Loke P, Wang X, Lloyd M, Ashley SE, Lozinsky AC, Gold M

Allergy. 2024 Oct;79(10):2759-2774. doi: 10.1111/all.16262. Epub 2024 Aug 4. PMID: 39099231

BACKGROUND

Few studies have examined long-term outcomes following oral immunotherapy (OIT); none have examined long-term risks and benefits associated with distinct clinical outcomes (desensitization, remission).

METHODS

Participants completing the probiotic and peanut oral immunotherapy (PPOIT) -003 randomized trial were enrolled in a follow-on study, PPOIT-003LT. Peanut ingestion, reactions, and health-related quality of life (HRQOL) were monitored prospectively. Outcomes at 1- year and 2-years post-treatment were examined by treatment group and by post-OIT clinical outcome (remission, desensitization without remission [DWR], allergic).

RESULTS

86% (151/176) of eligible children enrolled. Post treatment peanut ingestion at 2-years post-treatment were similar for PPOIT (86.7%) and OIT (78.7%) groups, both higher than placebo (10.3%). Reactions reduced over time for all treatment and clinical outcome groups (PPOIT 31.7% to 23.3%, OIT 37.7% to 19.7%, placebo 13.8% to 6.9%; remission 27.5% to 15.9%; DWR 57.9% to 36.8%; allergic 11.6% to 7%). At 2-years post-treatment, similar proportions of remission and allergic participants reported reactions (RD 0.09 (95%CI -0.03, 0.20), p = .127), whereas more DWR participants reported reactions than remission (remission vs DWR: RD -0.21 (95%CI -0.39; -0.03), p = .02) and allergic (DWR vs allergic: RD 0.30 (95%CI 0.13, 0.47), p = .001) participants. At 2-years post-treatment, 0% remission versus 5.3% DWR versus 2.3% allergic participants reported adrenaline injector usage. Remission participants had significantly greater HRQOL improvement (adjusted for baseline) compared with both DWR (MD -0.54 (95%CI -0.99, -0.10), p = .017) and allergic (MD -0.82 (95%CI -1.25, -0.38), p < .001).

CONCLUSION

By 2-years post-treatment, remission participants reported fewer reactions, less severe reactions and greater HRQOL improvement compared with DWR and allergic participants, indicating that remission is the patient-preferred treatment outcome over desensitization or remaining allergic.

3

Poco a poco se hace camino

Low-dose oral food challenges

Takei M, Yanagida N, Sato S, Ebisawa M

Pediatr Allergy Immunol. 2024 Oct;35(10):e14258. doi: 10.1111/pai.14258. PMID: 39396116

BACKGROUND & AIMS

Infants aged <1 year with confirmed food allergies generally need to avoid causative foods completely for a certain period. Low-dose oral food challenges (LD-OFCs) may be an effective strategy for safely introducing small amounts of causative foods to individuals with food allergies. This study clarified the safety of LD-OFCs in infants aged <1 year with food allergies.

METHODS

We retrospectively analyzed the clinical records of LD-OFCs performed in infants aged <1 year allergic to hen's egg, cow's milk, or wheat between April 2014 and October 2017. Approximately 1/25th 1/20th of the egg white from a heated whole hen's egg, 3 mL heated cow's milk, and 2 g wheat noodles (udon) were used as challenge foods. We examined the LD-OFC results, including the induced symptoms and treatment required for positive LD-OFC results.

RESULTS

The LD-Egg, LD-Milk, and LD-Wheat OFC groups comprised 68, 42, and 13 participants, respectively. The positivity rates for the LD-Egg, LD-Milk, and LD-Wheat OFC groups were 7%, 24%, and 0%, respectively. Patients predominantly exhibited skin symptoms, and most were treated with oral antihistamines alone. None of the patients experienced anaphylaxis or required adrenaline injections.

CONCLUSIONS

Infants aged <1 year with food allergies can safely undergo LD-OFCs by consuming low doses of causative foods. Avoiding the complete elimination of causative foods is an important strategy for managing infants with food allergies when initially introducing causative foods.

4

PROMovamos nuevas iniciativas para el paciente

Patient-Reported Outcome Measures in Rhinitis and Chronic Rhinosinusitis

Dykewicz MS, Wallace DV, Bandi S, Mahdavinia M, Sedaghat AR

J Allergy Clin Immunol Pract. 2024 Oct;12(10):2574-2582. doi: 10.1016/j.jaip.2024.06.049. Epub 2024 Jul 14. PMID: 39004415

ABSTRACT

Patient-reported outcome measures (PROMs) are valuable in the assessment and management of rhinitis and chronic rhinosinusitis (CRS). They measure outcomes that may include symptoms, disease control, well-being, and health-related quality of life (QOL). PROMs for rhinitis and rhinosinusitis are often used before and after an intervention, for example, medication, therapeutic procedure, or, in allergic rhinitis (AR), allergen immunotherapy. Although widely used in clinical trials for AR and conjunctivitis, symptom score PROMs are less validated than disease control or QOL measures. The best validated PROM for AR is the Rhinitis Quality of Life Questionnaire, but there is no universally accepted criterion standard for symptom and disease control PROMs. For CRS, at least 15 different criteria have been used to assess disease control in clinical studies, but what CRS disease control means and how it should be measured are concepts in evolution. The most used QOL measure for CRS is the 22-item Sinonasal Outcome Test. The use of PROMs to support clinical decisions and for shared decision-making for rhinitis and rhinosinusitis still has many challenges, including the selection of the preferred instrument, when and how to administer, the impact of comorbidities, and questionnaire fatigue for both patient and provider.

5

¿Hay relación entre la EEo, la rinitis y la administración de ITA?

Eosinophilic esophagitis and inhalant antigens: Pointing out the roles of allergic rhinitis, immunotherapy and biologic treatment

Erminia Ridolo, Francesca Nicoletta, Carlo Lombardi, Giovanni Passalacqua, Gianenrico Senna, Giorgio Walter Canonica

World Allergy Organ J. 2024 Sep 23;17(10):100968. doi: 10.1016/j.waojou.2024.100968. PMID: 39386073

ABSTRACT

Eosinophilic esophagitis (EoE) and allergic rhinitis (AR) usually represent the latest manifestations of the atopic march, sharing a common type 2 inflammation response. A relevant prevalence of AR in EoE cohorts has been widely confirmed. An increasing literature assessed the involvement of aeroantigens in EoE pathogenesis, focusing foremost on the seasonality of new diagnoses, symptoms, and response to therapy. Unfortunately, no diriment direction has been achieved, probably due to the retrospective design of the studies so far available, which chose surrogate markers of EoE activity (mostly the date of new diagnosis) which may be affected by geographical, logistic and personal factors, probably not dependent by the disease itself. EoE exacerbations reported in the context of the pollen levels (preferably pollen counts) may represent a more reliable marker. AR might promote the onset and the re-exacerbation of EoE through mechanisms that are both local (ie, massive exposure to airborne antigens mediated by post-nasal drip) and systemic (type 2 inflammation). Furthermore, AR may facilitate EoE onset by predisposing to pollen food allergic syndrome (PFAS), and EoE patients with PFAS reported higher rate of AR, thus suggesting a bond among these 3 conditions whose causative relationship have still to be ascertained. In addition, because of its shifting activity from Th2 to Th1 inflammation, several case reports focused on the effect of allergen immunotherapy (AIT) employed to treat AR in EoE patients. Also in this instance, no certainties could be guaranteed, although sublingual immunotherapy (SLIT) is more frequently reported to exacerbate EoE, while SCIT is mostly described as a remission adjuvant. The real life experience reported from our allergy service appears to confirm such hypothesis. Finally, a watchful eye should be reserved to monoclonal antibodies as a potential future option for concomitant EoE and AR. In light of all this, an attentive evaluation of allergic history of EoE patients should be relevant. Future perspectives should be addressed on prospective studies targeted to shed light on causative relations among airborne antigens, AR and EoE, and to viable comprehensive treatments.

6

La ITA, además, es coste-efectiva

Cost-effectiveness of allergen immunotherapy

Rodríguez-Otero N, Ramírez-Mateo E, Plana MN, Heffler E, Antolín-Amérigo D

Curr Opin Allergy Clin Immunol. 2024 Dec 1;24(6):496-503. doi: 10.1097/ACI.0000000000001028. Epub 2024 Oct 4. PMID: 39364915

PURPOSE OF REVIEW

Allergic rhinitis is a relevant and global health problem affecting up to 5-50% of the general population and its prevalence is increasing due to climate change and pollution among other factors and counts among the 10 most frequent reasons for medical consultation, generating an important economic impact. Allergen immunotherapy (AIT) is the only allergy-disease modifying treatment and there is plenty of evidence of its effectiveness with regards subcutaneous and oral routes of AIT.This narrative review article examines published literature in the last 24 months regarding the pharmacoeconomics of AIT versus standard of care treatment (SOC) for the treatment of allergic rhinitis and asthma.

RECENT FINDINGS

Farraia et al. assessed in 2022 subcutaneous immunotherapy (SCIT, _438/$500.28) and sublingual immunotherapy (SLIT) (_1021/$1116.19) plus symptomatic treatment versus SOC treatment in children with HDM-driven allergic asthma, measuring QALYs, decrease of medication, decrease of exacerbations and symptoms. They used the cost-effective threshold: _18 482.80 ($21 110.14), finding that AIT is cost-effective.Also, SCIT and SLIT plus symptomatic treatment was assessed versus SOC treatment in children with grass pollen allergic rhinitis. The authors concluded that SCIT (_933/$1065.67) and SLIT (_1408/ $1608.22) seem cost effective, particularly SCIT.

SUMMARY

Allergen immunotherapy is cost-effective in the management of allergic rhinitis and asthma as compared with SOC alone. As most studies consider only during-treatment costs and no long term benefits or preventive effects are being assessed, the real cost-effectiveness of allergen immunotherapy could be even higher.

7

ITA y asma: mejora la vía pequeña y disminuye la actividad del basófilo

Effect and mechanism of allergen-specific immunotherapy on small airway dysfunction in children with asthma

Zhong W, Ying X, Zhang L, Dong W, Lin J, Yang L, Hong L, Yin Y, Wu J

Pediatr Pulmonol. 2024 Oct 18. doi: 10.1002/ppul.27341. Epub ahead of print. PMID: 39422342

BACKGROUND

The purpose of this study was to investigate the effectiveness of allergen-specific immunotherapy (AIT) on small airway dysfunction (SAD) and the underlying mechanism with a special focus on basophils.

METHODS

Sixty-five children with mild to moderate asthma who were under regular inhaled corticosteroid (ICS) treatment for more than 1 year but whose FEF75 remained below 65% of the predicted value and had positive results for serum Der p or Der f were enrolled. Children with asthma underwent house dust mite (HDM) subcutaneous immunotherapy (SCIT) treatment for 1 year. Clinical symptoms and lung function were evaluated every 3 months during HDM SCIT treatment. Basophil activation test (BAT) was carried out before and after HDM SCIT treatment. RNA sequencing was performed in isolated basophils from peripheral blood after 6 months of HDM SCIT treatment, followed by GO term and KEGG pathway enrichment analysis between patients with and without HDM SCIT treatment.

RESULTS

HDM AIT treatment ameliorated clinical symptoms while concurrently improved lung function parameters, such as FEV1/FVC, FEF75, FEF50 and MMEF ($p < .05$). It is worth noting that FEF75 values showed a highly significant, gradual and persistent increase (from 49.55 ± 1.27% at baseline to 71.89 ± 2.64% after 1 year of therapy) and 22 of 35 patients no longer had SAD after 1 year of treatment. BAT results revealed that AIT treatment significantly reduced basophil activity to the inhalant allergen mixtures containing HDM in vitro challenge from baseline. GO term and KEGG pathway enrichment analysis of basophils revealed that downregulated genes were mainly involved in immune cell activation, antigen presentation, and Th2 cell differentiation.

CONCLUSIONS

Our study demonstrated that HDM AIT not only improved SAD related lung function parameters, but also reduced basophil activity. RNA sequencing revealed the inhibition of phagocytosis and the phagosome pathway in basophils which may affect the polarization of Th2 cell differentiation after HDM AIT.

8

Der p 2, marcador de efectividad de ITA

Predictive value of Der p 2-specific IgE for subcutaneous immunotherapy in children with allergic rhinitis

Wang J, Xu B, Jia X, He Y, Jia B, Li J, Xu M

Sci Rep. 2024 Oct 26;14(1):25467. doi: 10.1038/s41598-024-73575-6. PMID: 39461966; PMCID: PMC11513941

ABSTRACT

Dermatophagoides pteronyssinus (Der p) subcutaneous immunotherapy (SCIT) has demonstrated efficacy in clinical trials of childhood allergic rhinitis (AR). Currently, there is a lack of some generally accepted biomarkers that may predict the clinical response to SCIT to eventually achieve personalized therapy. In this study, 28 children with AR received Der p SCIT for 26-30 months at baseline, and four efficacy endpoints, serum interleukin (IL)-5, periostin, Der p-specific IgE (sIgE), and Der p sIgG4, were measured by ELSIA. Clinical symptoms and characteristics were assessed by questionnaires, and the associations among periostin, Der p 2 sIgE and clinical efficacy were analyzed. The results showed that SCIT demonstrated a significant reduction in Der p 1 sIgE ($P < 0.05$) and Der p 2 sIgE ($P < 0.01$), an increase in Der p sIgG4 ($P < 0.001$) and an improvement in clinical efficacy at the fourth efficacy endpoint compared with that at baseline. A positive linear correlation was found in serum periostin and Der p sIgE ($P < 0.05$), Der p sIgG4 ($P < 0.05$), and clinical efficacy. Importantly, the concentration of serum Der p 2 sIgE showed a positive linear correlation with clinical efficacy and serum periostin ($P < 0.05$). These results suggest that SCIT can result in reduced type 2 cytokines and Der p sIgE and has long-term efficacy in children with AR. Der p 2 sIgE has a positive linear correlation with clinical efficiency and serum periostin and may be a useful biomarker for the prediction of SCIT.

9

La ITA previene la aparición de asma

Allergen Immunotherapy for the Prevention and Treatment of Asthma

Batard T, Taillé C, Guilleminault L, Bozek A, Floch VB, Pfaar O, Canonica WG, Akdis C, Shamji MH, Mascarell L

Clin Exp Allergy. 2024 Oct 4. doi: 10.1111/cea.14575. Epub ahead of print. PMID: 39363801

ABSTRACT

Allergic asthma is the predominant phenotype among asthmatics. Although conventional pharmacotherapy is a central component in the management of asthma, it does not enable control of asthma symptoms in all patients. In recent decades, some uncontrolled asthmatic patients, especially those with allergic asthma, have benefited from biological therapies. However, biologics do not address all the unmet needs left by conventional pharmacotherapy. Furthermore, it is noteworthy that neither conventional pharmacotherapy nor biological therapies have disease-modifying properties. In this context, allergen immunotherapy (AIT) represents an indispensable component of the therapeutic arsenal against allergic asthma, due to its disease-modifying immunological effects. In this review article, funded by an AIT manufacturer, we find clinical trials support AIT as the only treatment option able both to improve allergic asthma symptoms and to prevent the onset and worsening of the condition. For patients with severe asthma or other safety concerns, the combination of AIT and biologics offers very promising new treatment modalities for the management of allergic asthma. Trial Registration: clinicaltrials.gov identifier: NCT06027073.

10

¿Cuál es el papel de la IA en alergología?

Future of Allergy and Immunology: Is AI the Key in the Digital Era?

Goktas P, Damadoglu E

Ann Allergy Asthma Immunol. 2024 Oct 18:S1081-1206(24)01595-3. doi: 10.1016/j.anai.2024.10.019. Epub ahead of print. PMID: 39428098

ABSTRACT

Artificial Intelligence (AI) is reshaping allergy and immunology by integrating cutting-edge technology to enhance patient outcomes and redefine clinical practices and research. This review examines AI's evolving role, emphasizing its impact on diagnostic accuracy, personalized treatments, and innovative research methodologies. AI has advanced diagnostic tools, such as models predicting allergen sensitivity, and enhanced immunotherapy strategies. Its ability to process extensive datasets has enabled deeper understanding of allergic diseases and immune system responses, leading to more accurate, effective and tailored treatments. Furthermore, AI is facilitating personalized care through AI-driven allergen mapping, automated patient monitoring, and targeted immunotherapy. The integration of AI into clinical practice promises a future where allergy and immunology are characterized by precisely customized healthcare solutions. This review adheres to PRISMA flowchart, with a comprehensive analysis of databases, including Scopus, Web of Science, PubMed, and preprint platforms using keywords related to AI and allergy and immunology. From an initial pool of 192 studies, 20 documents were selected based on inclusion criteria. Our findings highlight how AI is transforming allergy and immunology by enhancing patient care, research methodologies, and clinical innovation, offering a glimpse into the near future of technology-driven healthcare in these fields.

BBI BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Noviembre 2024

1

Cinco dosis de polimerizado con manano marcan la diferencia

Short-course subcutaneous treatment with birch pollen allergoids greatly improves symptom and medication scores in birch allergy

Ralph Mösges, Esther Raskopf, Ludger Klimek, Oliver Pfaar, Stefan Zielen et al

Allergy 2024 Nov 9. doi: 10.1111/all.16387

BACKGROUND

Subcutaneous immunotherapy has emerged as an effective option for treating allergic diseases. Here, we assessed the clinical impact of the mannan-conjugated birch pollen polymerized allergoid T502 in birch pollen-induced allergic rhinoconjunctivitis.

METHODS

In this prospective, randomized, double-blind placebo-controlled phase III trial, 298 birch pollen-allergic adult patients were treated across 28 trial sites in Germany. Patients received either placebo or 23,000 mTU T502 subcutaneously over five pre-seasonal visits. Efficacy was assessed by comparing the combined symptom and medication score (CSMS) between placebo and T502 during the peak birch pollen season 2022. Safety, tolerability and immunologic effects were also analyzed.

RESULTS

During the peak birch pollen season, the median CSMS of the T502 group was reduced by 33% ($p = 0.002$) compared to placebo. The median daily symptom score and daily medication score were reduced by 30.4% ($p < 0.001$) and 56.3% ($p = 0.045$), respectively. Health related quality of life improved as reflected by reduction of RQLQ values by 31.5% ($p < 0.0001$). Production of Bet v 1 sIgG4 and Bet v 1 sIgG increased up to 6.2-fold and 3-fold respectively in the T502 group ($p < 0.0001$). The sIgE/sIgG4 ratio was strongly reduced in the T502 group at V7 (-62.9%, $p < 0.0001$). No fatalities nor serious adverse events were reported. In total, 16 systemic allergic reactions occurred (Grade I/II).

CONCLUSIONS

Treatment with T502 significantly reduced symptoms and medication need in rhinoconjunctivitis patients. The treatment is well tolerated and safe.

2

Añade un poco de IL-2 y di adiós a la alergia

Low-dose IL-2 in birch pollen allergy: A phase-2 randomized double-blind placebo-controlled trial

Michelle Rosenzwajg, Alina Gherasim, Franck Dietsch, Marine Beck, Nathalie Domis et al

J Allergy Clin Immunol . 2024 Nov 10:S0091-6749(24)01181-3. doi: 10.1016/j.jaci.2024.10.033

BACKGROUND

Regulatory T (Treg) cells are pivotal in immune tolerance to allergens. Low-dose IL-2 (IL-2LD) activates Treg cells.

OBJECTIVE

Our aim was to assess IL-2LD efficacy for controlling clinical responses to allergen exposures.

METHODS

RHINIL-2 was a phase-2a, randomized, double blind, placebo-controlled trial. Patients with allergic rhinitis to birch pollen (BP) were included; 66% of them had concomitant asthma. All had a total nasal symptom score (TNSS) of 5 or more following nasal exposure to BP in an environmental exposure chamber. Patients received 1 MUI per day of IL-2 ($n = 12$) or placebo ($n = 12$) for 5 days, followed by weekly injections for 4 weeks. Clinical responses to subsequent BP exposures in the environmental exposure chamber were evaluated by using TNSS, the rhinitis visual analog scale (VAS), and spirometry. The primary efficacy end point was the difference in TNSS area under the curve (AUC) between inclusion and day 40.

RESULTS

IL-2LD treatment induced a significant expansion of Treg cells. The difference in TNSS AUC between inclusion and day 40 AUC in the IL-2 and placebo groups was not significant. TNSS and visual analog scale AUCs were significantly reduced from baseline to day 40 in the IL-2LD group only ($P = .04$ and $P = .01$, respectively). The ratio of FEV1 to forced vital capacity (FEV1P) and the forced midexpiratory flow (FEF25%-75%) showed improvement in the IL-2LD-treated versus in the groups given placebo at day 40 ($P = .04$ and $P = .04$, respectively). However, the short treatment duration used in this study could not have effects on specific IgE or IgG4 levels given their half-life. There were no severe treatment-related adverse events.

CONCLUSIONS

IL-2LD is well tolerated in patients with allergy, even in those with asthma, thus clearing the path for further therapeutic development. Our work suggests that Treg cells can safely attenuate an ongoing allergic response. It paves the way for larger studies with longer treatment periods, which are needed to properly evaluate the therapeutic potential of IL-2 in allergy.

3

Los comprimidos de abedul mejoran también a los niños

The SQ tree sublingual immunotherapy tablet is effective and well tolerated in children—A pivotal phase III trial

Monika Gappa, Rémi Gagnon, Fritz Horak, Ewa Cichocka-Jarosz, Terrie Dalgaard et al

Allergy . 2024 Nov 4. doi: 10.1111/all.16363

BACKGROUND

Allergic rhinitis and/or conjunctivitis (AR/C) induced by tree pollen is common and negatively impacts quality of life in children and adolescents. This phase III trial investigated the efficacy and safety of the SQ tree SLIT-tablet in a paediatric population (5-17 years) with moderate-to-severe AR/C induced by pollen from birch and trees in the birch homologous group.

METHODS

Nine hundred and fifty-two subjects were randomized (1:1) to daily treatment with SQ tree SLIT tablet or placebo for up to 52 weeks and had free access to AR/C symptom-relieving medications. The primary endpoint was the average total combined score (TCS); sum of average daily symptom score (DSS) and average daily medication score (DMS) during the birch pollen season (BPS). Key secondary endpoints included average DSS and DMS during BPS and average TCS, DSS and DMS during tree pollen season (TPS).

RESULTS

SQ tree SLIT-tablet demonstrated a statistically significant and clinically relevant treatment effect compared with placebo for the TCS during BPS with an absolute treatment difference of 1.29 (95% CI: 0.58, 2.00; p = .0004) and a relative reduction of 21.9% (95% CI: 10.6, 31.9). Results were substantiated by reductions in both DSS and DMS versus placebo during the BPS and in DSS, DMS and TCS during the TPS. Treatment was generally well tolerated. Most treatment-related adverse events were mild or moderate local administration site reactions.

CONCLUSION

This is the first paediatric trial to provide robust evidence of efficacy and safety of the SQ tree SLIT-tablet in tree polleninduced AR/C in a paediatric population (5-17 years).

4

“Los comprimidos de gramíneas 300-IR son efectivos” (palabra de metaanálisis)

A 300 IR 5-grass pollen sublingual immunotherapy tablet-specific systematic review and meta-analysis confirms its clinical benefits for patients with allergic rhinoconjunctivitis with or without asthma

Danilo Di Bona, Giovanni Paoletti, Michal Ordak, Silvano Dragonieri, Josiane Cognet-Sice

World Allergy Organ J. 2024 Oct 24;17(11):100985. doi: 10.1016/j.waojou.2024.100985

BACKGROUND

In the realm of allergen immunotherapy (AIT), the quality of evidence varies across different products, making it unjustifiable to extend overall conclusions to all AIT products, as highlighted by WAO and EAACI.

OBJECTIVE

To confirm the efficacy of the 300 IR 5-grass pollen sublingual AIT (SLIT)-tablet through a specific meta analysis of randomized controlled trials (RCTs) involving patients with allergic rhino conjunctivitis (ARC) with/without mild/intermittent asthma.

METHODS

Data from published RCTs on the 300 IR 5-grass SLIT-tablet were gathered from electronic databases (MEDLINE, ISI Web of Science, LILACS, the Cochrane Library and ClinicalTrial.gov) and manual searches up to November 2023. Populations, treatments, and outcome data were combined. Efficacy was assessed based on symptom score (SS) and medication score (MS), measured as standardized mean difference (SMD) or mean difference (MD).

RESULTS

Results from 5 RCTs comprising 1468 patients revealed a significant reduction in SS (SMD, -0.36; 95%confidence interval [CI], - 0.52 to -0.19; P < 0.05) and MS (SMD, -0.29; 95%CI, -0.40 to -0.19; P < 0.05) compared to placebo. The difference of -0.36 SMD for SS corresponds to a MD of -1.26 SS points, greater than the minimal important difference. Subgroup analysis did not show differences in efficacy according to age, asthma status, and geographic location of the study (USA, Canada, Europe, Russia). No safety issues were reported.

CONCLUSION

This product-specific meta-analysis reinforces the evidence of clinical benefits associated with the 300 IR 5-grass SLIT tablet, suggesting its appropriateness as a therapeutic choice for patients with ARC, irrespective of concurrent asthma, and exhibiting a favorable safety profile.

5

Pauta cluster con depot de ácaros, más reacciones locales pero segura y bien tolerada

One-strength dose escalation of house dust mite depot product for subcutaneous immunotherapy is safe and tolerable

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Allergy. 2024 Nov 14. doi: 10.1111/all.16370

BACKGROUND

Allergen immunotherapy (AIT) aims at modulating the immune response by administration of allergen preparations at regular intervals over several years (1). For subcutaneous AIT (SCIT), the treatment is initiated with a dose escalation phase followed by a maintenance dose administration. Over the last decade, there has been a trend towards shortening dose escalation regimens to increase patient adherence. This open-label, phase II trial aimed to investigate the safety and tolerability of a house dust mites (HDMs) SCIT product when used in a newly designed one-strength dose escalation scheme.

METHOD

Patients, aged 12-65, suffering from HDM-allergic rhinitis/rhinoconjunctivitis ± asthma were included. Patients were randomized to the one-strength (6 injections from the highest strength 3) or the Standard dose escalation regimen (14 injections from strengths 1 to 3) using the HDMs-SCIT product. All adverse events were reported. Tolerability was assessed on the Likert scale.

RESULTS

One hundred and forty-three patients were randomized, 79 adults and 64 adolescents. In total, the one-strength regimen caused more adverse drug reactions (ADRs) than the Standard regimen (p = .0457). With both regimens most ADRs were local reactions which occurred more often in the one-strength group (p = .0393). But there was no significant difference in the number of patients affected by systemic or serious ADRs between both regimens. No relevant differences occurred between the two age groups and no other risks were observed for adolescents compared to adults.

CONCLUSION

The safety and tolerability of both regimens can be considered comparable, as most ADRs were local reactions, primarily rated as mild in intensity. Nevertheless, the one-strength regimen caused more ADRs. Reducing the number of injections from 14 to 6 while using only one strength offers the potential to improve patient adherence which further might increase clinical efficacy. Future trials could confirm this hypothesis.

6

Consenso internacional sobre el manejo del síndrome polen-frutas

An International Delphi Consensus on the Management of Pollen-Food Allergy Syndrome: A Work Group Report of the AAAAI Adverse Reactionsto Foods Committee

Taha Al-Shaikhly, Amanda Cox, Anna Nowak-Wegrzyn, Antonella Cianferoni, Constance Katelaris, et al

J Allergy Clin Immunol Pract . 2024 Dec;12(12):3242-3249.e1. doi: 10.1016/j.jaip.2024.09.037. Epub 2024 Nov 2

BACKGROUND

Pollen-food-allergy syndrome (PFAS) is common among patients with allergic rhinitis. Treatment recommendations for patients with PFAS remain variable.

OBJECTIVE

To develop consensus recommendation statements for managing patients with PFAS.

METHODS

An international panel of allergists, researchers, and nutritionists with an interest in PFAS from 25 different institutions across 11 countries convened and a list of statements was written by 3 authors. The RAND/University of California Los Angeles methodology wasadopted to establish consensus on the statements.

RESULTS

After 2 Delphi rounds, a consensus was reached on 14 statements. The panel agreed that patients with PFAS would benefit from counseling on the nature and basis of PFAS and the rare chance of more severe systemic reactions and their recognition. The panel agreed on avoiding the raw food responsible for the index reaction, but not potentially cross-reactive fruits/vegetables based on the responsible food of the index reaction. Epinephrine autoinjectors should be recommended for patients with PFAS who experienced severe symptoms (beyond the oropharynx) or for patients considered at risk for severe reactions. The panel agreed that the benefit of allergen immunotherapy remains unclear and that PFAS should not be considered the primary indication for such intervention.

CONCLUSIONS

We developed consensus statements regarding counselling patients about the nature and severity of PFAS, potential risk factors, dietary avoidance, epinephrine autoinjector prescription, and allergen immunotherapy consideration for patients with PFAS.

7

La IT intralinfática a examen: mejora la calidad de vida, pero no los síntomas

Is intralymphatic immunotherapy effective and safe for allergic rhinitis?: A meta-analysis

Liangrong Liu, Yacheng Liang, Le Yan, Zhiyong Li

Medicine (Baltimore). 2024 Nov 15;103(46):e40589

BACKGROUND

As there is much controversy in using intralymphatic immunotherapy (ILIT) as a therapeutic means for allergic rhinitis (AR), its efficacy and safety for AR were investigated based on a systematic review and meta-analysis.

METHODS

Databases PubMed, Embase, Cochrane library, and Web of Science were employed to retrieve relevant randomized control studies on ILIT for AR. The search deadline was September 15, 2023. Meta-analysis was performed on the data of the included literature using Stata 15.0.

RESULTS

Eleven randomized control studies were included involving a total of 406 patients. Meta-analysis results revealed that ILIT improved patients' quality of life [standardized mean difference (SMD) = -0.53, 95% confidence interval (CI) = (-1.00, -0.050)], and reduced the adverse events of nasal symptoms [risk ratio (RR) = 0.16, 95% CI = (0.06, 0.45)] as compared to control, whereas no significant difference was discovered in symptom score [SMD = 0.14, 95% CI = (-0.34, 0.62)], IgE [SMD = 0.93, 95% CI = (-0.44, 2.30)], medication scores [SMD = 1.37, 95% CI = (-0.45, 3.18)], comprehensive symptom and medication scores [SMD = 0.93, 95% CI = (-0.62, 2.47)], nasal symptoms [RR = 0.16, 95% CI = (0.06, 0.45)], and lymphadenectasis [RR = 2.27, 95% CI = (0.37, 6.73)] versus control.

CONCLUSION

After the application of the ILIT strategy against AR, the quality of life of patients was improved and the incidence of adverse events associated with nasal symptoms was reduced, but the conclusion needed further verification with more high quality research.

8

¿Cómo usar las nanopartículas para la rinitis?

Application of Nanoparticles for Immunotherapy of Allergic Rhinitis

Kaiqiang Li, Jing Jin, Yimin Yang, Xuling Luo, Yaling Wang

Int J Nanomedicine . 2024 Nov 18:19:12015-12037. doi: 10.2147/IJN.S484327

ABSTRACT

Allergen Immunotherapy (AIT) is the only etiological therapeutic method available for allergic rhinitis (AR). Currently, several options for AIT in the market, such as subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT), have different routes of administration. These traditional methods have achieved encouraging outcomes in clinic. However, the side effects associated with these methods have raised the need for innovative approaches for AIT that improve safety, shorten the course of treatment and increase local drug concentration. Nanoparticles (NPs) are particles ranging in size from 1 to 100 nm, which have been hired as potential adjuvants for AIT. NPs can be employed as agents for modulating immune responses in AR or/and carriers for loading proteins, peptides or DNA molecules. This review focuses on different kinds of nanoparticle delivery systems, including chitosan nanoparticles, exosomes, metal nanoparticles, and viral nanoparticles. We summarized the advantages and limitations of NPs for the treatment of allergic rhinitis. Overall, NPs are expected to be a therapeutic option for AR, which requires more in-depth studies and long-term therapeutic validation.

9

El mejor biomarcador en ITA con venenos es ... ¡la suma de dos!

Monitoring and stopping Hymenoptera venom immunotherapy: Contribution of IgE blocking activity

Julie Poulat, Elisabeth Bellet-Fraysse François Touraine, Camille Coumes-Salomon, Boris Melloni

J Allergy Clin Immunol Glob. 2024 Aug 24;3(4):100329. doi: 10.1016/j.jacig.2024.100329

BACKGROUND

Hymenoptera venom allergy is a public health issue and has an undeniable impact on quality of life. Allergen immunotherapy (AIT) has shown long-term efficacy in this severe and potentially lethal allergy. However, no biomarker can predict the effectiveness of this treatment.

OBJECTIVES

We evaluated the contribution of IgE blocking activity, a functional biomarker carried out in our center using flow cytometry, to predict the efficacy of AIT.

METHODS

This retrospective study from 1985 to 2022 describes in detail the demographic, clinical, and biological characteristics of patients who benefited from AIT with Hymenoptera venom at the University Hospital of Limoges. The outcome measure used was the presence of anaphylactic reaction (grade I to IV according to Ring and Messmer) in case of a new sting after discontinuation of AIT.

RESULTS

Our study, mainly composed of patients allergic to Vespula wasp venom, did not emphasize the interest of IgE blocking activity in the prediction of a relapse after a new sting. However, this inhibition showed a significant correlation with the amount of IgG4 antibodies.

CONCLUSION

There is no biomarker that can help make the decision of stopping AIT. However, low levels of IgE blocking activity may suggest a likelihood of relapse. Serum IgG4, in correlation with IgE blocking activity, could be useful for monitoring treatment response. Additional studies are necessary to gain a thorough understanding of the composition of inhibitory antibodies.

10

La “36γ” es la interleuquina para medir efectividad en ITA

Sublingual Immunotherapy Decreased the Serum Levels of Interleukin-36γ in Allergic Rhinitis

Xiaowei Qin, Chunrui Wang, Jueqi Li, Xiaopeng Zhang, Tianhong Zhang

Mediators Inflamm. 2024 Nov 6:2024:9692031. doi: 10.1155/2024/9692031

BACKGROUND

Allergy immunotherapy (AIT), a treatment approach for allergic rhinitis (AR), is recognized for its potential to modify the disease course beyond mere symptom relief. Interleukin 36γ (IL-36γ), a key player in immune responses, has been implicated in promoting eosinophilic inflammation in AR by activating eosinophils. We aimed to investigate the effect of IL-36γ on group II lymphoid cell (ILC2) in AR patients who underwent sublingual immunotherapy (SLIT).

METHODS

Twenty-four AR patients were enrolled and administered with SLIT. Serum proteins of IL-36γ, interleukin-5 (IL-5), and interleukin-13 (IL-13) during SLIT were quantitatively assessed using enzyme-linked immunosorbent assay (ELISA). The proportion of ILC2 was determined by flow cytometry. Sorted ILC2s were stimulated by IL-36γ and ILC2 cell differentiation, and type II cytokines expression were examined.

RESULTS

SLIT treatment decreased the serum protein levels of IL-36γ, IL-5, IL-13, and the proportion of ILC2 significantly. IL-36γ suppressed the proliferation of ILC2 by inhibiting the levels of ILC2 transcription factor. IL-36γ also inhibited IL-5 and IL-13 expression from ILC2.

CONCLUSION

The changes of IL-36γ during SLIT were related to the inhibited function of ILC2, implying that IL-36γ may be used as a new biomarker for monitoring the efficacy of SLIT in AR.

BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Diciembre 2024

1

Lo importante es el equilibrio

Allergen-Specific Immunotherapy and Trained Immunity

Martín-Cruz L, Palomares O

Allergy. 2024 Dec 6. doi: 10.1111/all.16423. Epub ahead of print. PMID: 39641571

ABSTRACT

The high prevalence of allergic diseases reached over the last years is attributed to the complex interplay of genetic factors, lifestyle changes, and environmental exposome. Allergen-specific immunotherapy (AIT) is the single therapeutic strategy for allergic diseases with the potential capacity to modify the course of the disease. Our knowledge of the mechanisms involved in allergy and successful AIT has significantly improved. Recent findings indicate that long-term allergen tolerance upon AIT discontinuation not only relies on the generation of proper adaptive immune responses by the generation of allergen-specific regulatory T and B cells enabling the induction of different isotypes of blocking antibodies but also relies on the restoration of proper innate immune responses. Trained immunity (TRIM) is the process by which innate immune cells acquire memory by mechanisms depending on metabolic and epigenetic reprogramming, thus conferring the host with increased broad protection against infection. This concept was initially explored for infectious diseases, as well as for vaccination against infections, but compelling experimental evidence suggests that TRIM might also play a role in allergy and AIT. Hyperinflammatory innate immune responses in early life, likely due to TRIM maladaptations, lead to aberrant type 2 inflammation-enhancing allergy. However, exposure to farming environments and specific microbes prevents recurrent infections and allergy development, likely due to mechanisms partially depending on TRIM. TRIM-based vaccines and next generation AIT vaccines inducing metabolic and epigenetic reprogramming in innate immune cells and their precursors have shown protective antiallergic effects. A better understanding of the factors involved in early-life TRIM mechanisms in the context of allergy and the identification and characterization of novel tolerance inducers might well enable the design of alternative TRIM-based allergen vaccines for allergic diseases.

2

El mejor predictor de remisión en alergia a cacahuete sigue siendo el nivel de IgE específica

Allergen Specific IgE is a Stronger Predictor of Remission Following Peanut Oral Immunotherapy Than Age in Children Aged 1-10 Years

Sarah E Ashley, Melanie Lloyd, Paxton Loke, Francesca Orsini, Adriana C Lozinsky, et al

Allergy. 2024 Dec 26. doi: 10.1111/all.16451. Online ahead of print

BACKGROUND

Remission is the desired outcome following OIT as it allows individuals to discontinue treatment and eat the allergen freely. Early initiation of OIT in infants and toddlers has been embraced as an approach to increase the likelihood of remission. However, there is no high-quality evidence supporting younger age as an independent factor driving remission; available studies are limited by small samples of younger subjects and lack of adjustment for confounding covariates, particularly peanut-specific IgE (sIgE) levels which is closely correlated with age.

METHODS

This study examined relationships between peanut sIgE and age at baseline and remission, in children aged 1-10 who completed 18 months of OIT in the PPOIT-003 RCT (n = 162). Remission was defined as absence of clinical reactivity to peanut after 8 weeks of allergen avoidance/treatment discontinuation. Age and sIgE were examined as continuous variables in univariate and multivariate regression models.

RESULTS

Higher peanut sIgE was consistently predictive of lower likelihood of remission, independent of age. In contrast, there was no independent association between age and remission after adjusting for baseline sIgE (OR 0.94 [0.79-1.12], p = 0.5).

CONCLUSIONS

Findings do not support age as an independent predictor of remission following OIT. Additional studies examining safety and efficacy of OIT in infants and younger children are urgently needed, ahead of widespread adoption of early intervention.

3

Añadir dupilumab mejora a la ITO en la alergia a cacahuete

Dupilumab as an Adjunct to Oral Immunotherapy in Pediatric Patients With Peanut Allergy

Chinthrajah RS, Sindher SB, Nadeau KC, Leflein JG, Spergel JM, et al

Allergy. 2024 Dec 14. doi: 10.1111/all.16420. Epub ahead of print. PMID: 39673367

BACKGROUND

Peanut allergy is a common, life-threatening food allergy in children. We evaluated whether dupilumab, which blocks the activity of interleukin (IL)-4/IL-13, enhances the efficacy of oral immunotherapy (OIT) AR101 in pediatric patients with peanut allergy.

METHODS

A Phase II, multicenter, randomized, double blind study was conducted in the USA (NCT03682770) in pediatric patients (6-≤ 17 years old) with confirmed peanut allergy. Patients were randomized 2:1 to receive dupilumab + OIT or placebo + OIT during a 28-40-week up-dosing period. Patients in the dupilumab + OIT group were re randomized 1:1 and received dupilumab + OIT or placebo + OIT during 24-week OIT maintenance, undergoing a 2044 mg (cumulative) of peanut protein double-blind, placebo-controlled food challenge (DBPCFC) following up-dosing, maintenance, and at 12-week post-treatment follow-up.

RESULTS

The study enrolled 148 patients, 123 of whom were included in the modified full analysis set, with a mean age of 11.1 years. Dupilumab + OIT treatment (n = 84) led to a 20.2% increase ($p < 0.05$) in the number of patients who passed a DBPCFC to 2044 mg (cumulative) of peanut protein following the up-dosing period versus placebo (OIT alone, n = 39). Following the OIT maintenance period, continuous dupilumab treatment improved the number of patients who passed a DBPCFC to 2044 mg (cumulative) of peanut protein versus patients continuously on OIT alone (16.6% difference [95% CI -9.7, 42.8], $p = 0.2123$). Safety was consistent with known dupilumab safety profile.

CONCLUSIONS

Dupilumab provided a modest increase efficacy of OIT in children and adolescents with peanut allergy, though it did not provide protection against OIT-related anaphylaxis.

4

Cuantas más (sensibilizaciones), peor (pronóstico)

Molecular allergen sensitization drives phenotypes of severe asthma in children: Evidence from a megacity cohort (SAMP)

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Pediatr Allergy Immunol. 2024 Dec;35(12):e70014. doi: 10.1111/pai.70014

BACKGROUND

Several major sensitization profiles have been described in children with asthma, but it remains unclear how these profiles relate to asthma phenotypes. The aim of this study was to determine allergenic sensitization profiles in a megacity cohort (SAMP).

METHODS

This was a cross-sectional analysis performed from 2011 to 2015 including preschool and school-age children with severe and moderate asthma from the SAMP cohort. We performed ALEX multiplex array and carried out cluster analysis.

RESULTS

Data from 367 children were analyzed: 224 of preschool age and 143 of school age, respectively 84 (38%) and 114 (80%) presented at least one allergic sensitization. At preschool age, three clusters were identified: Cluster 1, Few sensitizations to inhaled allergen molecular families and nontype 2 (T2) inflammation (n = 61); Cluster 2, Predominant sensitization to HDM molecular families (n = 16); Cluster 3, Severe asthma with multiple sensitizations to inhaled and food allergen molecular families (n = 7). At school age, five clusters were identified: Cluster 1, Few sensitizations to inhaled allergen molecular families and non-T2 inflammation (n = 43); Cluster 2, Predominant sensitization to HDM molecular families (n = 31); Cluster 3, Predominant sensitization to PR-10 protein family (n = 25); Cluster 4, Severe asthma with predominant sensitization to tropomyosin family (n = 11); Cluster 5, Severe asthma with multiple sensitizations to inhaled and food allergen molecular families (n = 4).

CONCLUSION

These results underline the heterogeneity of sensitization profiles in severe allergic childhood asthma. The most severe asthma phenotypes were associated with multiple sensitizations to both inhaled and food allergen molecular families as expected, and to the tropomyosin molecular family, a novel finding.

5

¿Modificar los alérgenos con inmunosupresores para hacerlos más eficaces?

α2-3 Sialic acids-decorated allergens exert a tolerogenic effect on CD4 T cells from Der p 2 - allergic patients

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Int Arch Allergy Immunol. 2024 Dec 19:1-19. doi: 10.1159/000543157

BACKGROUND

Allergen-specific immunotherapy (AIT) is so far the only disease-modifying therapy for allergy, resulting in a long lasting tolerance. However, the existing safety concerns and the need for more efficacious alternatives that shorten the duration of treatment have stimulated research into the development of novel alternatives. Some of these novel alternatives involve modifying allergens with molecules that target innate immunomodulatory receptors to suppress the immune activity of immune cells.

METHODS

Freshly prepared monocyte-derived dendritic cells (moDCs) from mite-allergic and non-atopic volunteers were treated with α2-3 sialic acidconjugated recombinant Der p 2 ((sia)-Der p 2) and unconjugated Der p 2 in culture and matured with Toll-like receptor (TLR) 1/2 (Pam3CSK4) (Pam3) and 2/4 (lipopolysaccharide) (LPS) agonists, followed by co-culture with autologous CD4+ T cells. Secretion of cytokines in supernatants were measured by ELISA and expression of cell surface and intracellular markers was measured by flow cytometry.

RESULTS

Sia-Der p 2 unlike Der p 2, modulated moDCs from mite-allergic volunteers by reducing expression of CD83 and CXCR5. We also observed that sia-Der p 2-treated moDCs in the presence of Pam3 and LPS significantly suppressed the proportion of CD25+, Ki67+, IL-13+ and IFN-y+ CD4+ T cells of mite-allergic volunteers while Der p 2-treated moDCs did not. Sia-Der p 2-treated moDC did not alter these CD4+ T cell populations in non-atopic volunteers.

CONCLUSION

Our data suggests that Der p 2 conjugated with α2-3 sialic acids modifies moDCs and promotes the differentiation of allergen specific CD4+ T cells towards a regulatory profile.

6

Midamos la eficacia de la ITA para rinitis en la nariz

Nasal secretions trace epithelial type 2 response to allergen-specific immunotherapy

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Rhinology. 2024 Dec 11. doi: 10.4193/Rhin24.038

BACKGROUND

Allergen-specific immunotherapy (AIT) is a disease modifying therapy and is effective to reduce the symptoms of grass pollen-allergy. The airway epithelium of these patients releases inflammatory mediators including type-2 cytokines, which are associated with cellular processes involved in the symptomatic response of the affected tissue. Aim of the study was to identify epithelial biomarkers indicating AIT progress.

METHODS

In an exploratory, observational allergy cohort, we longitudinally phenotyped 56 grass pollen-allergic patients undergoing AIT for over three years and 18 controls using nasal secretions at critical time windows during therapy to assess peak-season responses along the course of therapy. Type-2 cytokine protein levels were analyzed using the high-sensitivity multiplex electrochemiluminescence mesoscale technique.

RESULTS

The type-2 cytokines CCL26 and POSTN oscillated seasonally, in contrast to TSLP and IL-33. However, only POSTN was reduced over the three-year AIT progression. In addition to POSTN, IL-24 and IL-37 levels were continuously reduced during AIT, while IFN-g and CCL27 were increased. Compared to healthy individuals, AIT did not restore healthy secretion levels but rather induced a novel homeostasis.

CONCLUSION

Nasal secretions trace the epithelial response during different phases of AIT. We demonstrate that AIT only partially controls the epithelial type 2 cytokine CCL26, which also adapts to seasonal changes, while POSTN and IL-24 are potential indicators of therapy success. Therefore, nasal secretions represent a promising, non-invasive tool for monitoring seasonal progress of AIT.

7

La escalera de la leche peldaño a peldaño

Milk ladder: Who? When? How? Where? with the lowest risk of reaction

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Front Allergy. 2024 Dec 6;5:1516774. doi: 10.3389/falgy.2024.1516774. PMID: 39713044; PMCID: PMC11659236

ABSTRACT

The milk ladder (ML) approach, which is the gradual reintroduction of the milk allergen from the least allergenic forms to the most allergenic forms into the diet of the patients, has been utilized mostly in non IgE-mediated but in some countries also in IgE-mediated CMPA due to its possible benefits which include nutrition, quality of life and tolerance induction. Despite increasing interest, so far, there is no guideline on ML; thus, the use of this approach shows discrepancies among healthcare professionals as many factors such as dietary habits, patient history, test results, workload, and facilities of the hospitals, the anxiety of the parents/patients may affect the decision on how, when, where and whom to use ML. Here, we reviewed current data on implementing the ML, suggested a 4-step ML including receipts and amounts, and shared our experience on optimal patient selection, appropriate time and steps for initiating ML, and time intervals between the steps targeting the lowest risk of reaction. We also added the newly developed twice-baked biscotti cake to the ML. We presented the analyses of this product, showing its low allergenicity compared to conventional cake, which provides a safer introduction of milk into the diet.

8

Las dosis altas también son seguras

Clinical Trial With a Depigmented, Polymerized Mite Mixture Extract at Maximum Concentrations

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Immun Inflamm Dis . 2024 Dec;12(12):e70090. doi: 10.1002/iid3.70090

BACKGROUND

Efficacy of allergen immunotherapy is dose dependent; however, high doses of allergen may imply a greater risk of adverse reactions.

OBJECTIVE

To assess the safety and tolerability of subcutaneous immunotherapy (SCIT) with mixtures of mite allergen extracts, Dermatophagoides pteronyssinus/Blomia tropicalis (Dpt/Bt) and Dermatophagoides pteronyssinus/Lepidoglyphus destructor (Dpt/Ld) at maximum concentrations, in adult patients with allergic rhinitis or rhinoconjunctivitis, and controlled allergic asthma due to a clinically relevant sensitisation to these mites.

METHODS

An open-label, noncontrolled, nonrandomised, phase IIb clinical trial was carried out in three hospitals in Spain between September 2014 and May 2018. Patients received SCIT of either Dpt/Bt (100/1000 DPP/mL) or Dpt/Ld (100/100 DPP/mL) in two phases: a rush build-up phase on the first day (0.2 mL and 0.3 mL with a 30-min interval) and a monthly maintenance phase administration (0.5 mL) up to 48 months.

RESULTS

Forty patients were recruited for the study, seven allocated to the Dpt/Bt group and 33 to the Dpt/Ld. None experienced immediate or delayed systemic Grade ≥ 2 reactions (EAACI classification) (systemic reactions were mostly Grade 1) nor died during the study. Local reactions were mostly mild (0–10 cm). Thirty-nine patients (97.5%) experienced at least one adverse event (AE). Of the 283 reported AEs, eight (2.8%) were systemic reactions experienced by six (15%) subjects and 14 (4.9%) were local reactions sustained by ten (25%) subjects.

CONCLUSIONS

SCIT treatment of patients with allergic rhinitis or rhinoconjunctivitis and controlled asthma with mixtures of Dpt/Bt and Dpt/Ld allergen extracts at maximum concentrations showed a favourable safety profile.

9

¿Qué hacer con los niños alérgicos a veneno de himenópteros?

Hymenoptera venom allergy in children

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Ital J Pediatr. 2024 Dec 20;50(1):262. doi: 10.1186/s13052-024-01731-9

ABSTRACT

From a taxonomic point of view, Hymenoptera are subclassified into families: Apidae, including honeybees (Apis mellifera) and bumblebees (Bombus), and Vespidae, which, in turn, are divided into the subfamilies of Vespinae (wasps, including hornets, vespules, dolichovespules) and Polistinae (paper wasp). Hypersensitivity to Hymenoptera venom can be linked to immunological (IgE-mediated or non-IgE mediated) and non-immunological mechanisms. Reactions are classified into local reactions, large local reactions, systemic reactions, toxic reactions, and unusual reactions. In general, children sensitize less frequently and have less severe reactions than adults, probably due to less exposure to repeated stings and fewer comorbidities. There are risk factors for systemic reactions that should be discussed with patients and their parents as appropriate. A correct diagnosis of Hymenoptera venom allergy relies on a careful clinical history and the appropriate use of skin and in vitro tests. The in vitro tests include serum specific IgE toward venom extracts and toward allergenic molecules. In complex diagnoses, CAP-inhibition and the Basophil Activation Test can also be used. In the presence of a systemic reaction, the basal serum tryptase measurement should be performed to rule out mastocytosis. In case of allergic reactions to Hymenoptera stings, in the acute phase, according to the current guidelines, the treatment of signs and symptoms mainly includes the use of adrenaline as first-line treatment in case of anaphylaxis and antihistamines and corticosteroids as subsequent lines of treatment. Given the impossibility of avoiding a new sting with certainty, the treatment of choice in subjects with hypersensitivity to Hymenoptera venom who have experienced systemic reactions is based on venom immunotherapy (VIT), with the venom of the responsible stinging insect identified after an adequate allergological work-up. VIT is performed in a suitable environment and has proved to be safe and effective with various administration protocols, both accelerated and conventional. The prevention of Hymenoptera venom anaphylaxis in patients who have already developed a previous episode is crucial and must be supported by environmental protection interventions and early therapy. Places where one is more likely to encounter insects and risky behaviors should be avoided.

10

ITO u omalizumab en alergia a alimentos, esa es la cuestión

Treatment of food allergy: Immunotherapy, omalizumab, or both

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J Allergy Clin Immunol Pract. 2024 Dec 17:S2213-2198(24)01253-4. doi: 10.1016/j.jaip.2024.12.011

ABSTRACT

Food allergy is a common disease which has substantial impacts on the quality of life of patients and their families, and all reactions have the potential for causing life-threatening anaphylaxis. Food allergic individuals currently have 2 FDA approved therapeutic options available to them aside from lifelong allergen avoidance: oral immunotherapy (OIT), and omalizumab. OIT for food allergy has been extensively studied in clinical trials and currently provides the greatest level of protection, however it also has a high burden of treatment. Studies suggest that more successful OIT outcomes may be attained with earlier intervention; however, early OIT presents its own challenges. Omalizumab, recently FDA approved, is a biologic targeting immunoglobulin E, a major driver of allergic reactions. In contrast to OIT, omalizumab monotherapy offers a low treatment burden therapeutic option that provides a safety net against reactions to accidental ingestion to multiple allergens. Additionally, omalizumab has also been investigated as an adjunct to OIT, improving the speed and safety of single or multi allergen OIT. Here we discuss the clinical use of these therapeutic options and provide a guide for shared decision-making between patients and physicians about what therapeutic option might be more appropriate.